METABOLIC DERANGEMENTS IN PAEDIATRIC DIABETIC KETOACIDOSIS IN A TERTIARY CARE HOSPITAL

Dissertation submitted to

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI

In partial fulfilment of the regulations for the award of degree of

M.D. (PAEDIATRICS)

(BRANCH VII)

INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN

MADRAS MEDICAL COLLEGE

CHENNAI

APRIL – 2016

CERTIFICATE

This is to certify that dissertation entitled "**METABOLIC DERANGEMENTS IN PAEDIATRIC DIABETIC KETOACIDOSIS IN A TERTIARY CARE HOSPITAL"** submitted by Dr.Hamza M to the faculty of paediatrics, The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the award of M.D. Degree (Paediatrics) is a bonafide research work carried out by her under direct supervision and guidance.

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DECLARATION

I Dr. Hamza M solemnly declared that the dissertation titled "**METABOLIC DERAGEMENTS IN PAEDIATRIC DIABETIC KETOACIDOSIS IN A TERTIARY CARE HOSPITAL**" has been prepared by me. This is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the rules and regulations for the M.D degree examination in paediatrics.

Dr.HAMZA. M

DATE :

PLACE :

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ABSTRACT

METABOLIC DERANGEMENTS IN PAEDIATRIC DIABETICKETOACIDOSIS IN A TERTIARY CARE HOSPITAL

Hamza M, Sridevi A Naaraayan. MD, D. Prabhakar. MD, Priyadharshini.D. MD

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OBJECTIVES:

To study the metabolic derangements in pediatric DKA in 1st 48 hours of admission and to determine its relation as well as the relation of sepsis with duration of insulin infusion and hospital stay.

METHODS:

This descriptive study was conducted in the paediatric intensive care department of ICH& HC between Jan 2015 to Sep 2015. All children who were admitted to the intensive care unit with DKA were included while those who were partially treated in outside hospitals for DKA were excluded. After obtaining informed consent from parent, patient details including demographic details, family history, pre existent diabetes, precipitating cause and anthropometric parameters were noted in a structured proforma. Venous blood was drawn for investigation such as renal function test and electrolytes and arterial blood gas analysis was also done. All the investigations were done at admission and after 12, 24, 36, 48 hrs. The duration of insulin infusion and hospital stay and outcome were also noted down. This data was analyzed using SPSS version 20. Continuous variables were converted into categorical variables and reported as proportion. Duration of insulin infusion and duration of hospital stay in various categories were analysed using box and whisker plot

RESULTS:

Total of 33 patients were included in the study. Of these 51.5% were more than 10 years of age and the male female ratio was 1.06:1. 36% of cases occurred in those with pre existing diabetes while the rest 64% were new onset diabetes. Family history of diabetes mellitus was present only in 27%. In majority (49%) of cases the

precipitating cause of DKA could not be identified and infection was the most common (42%) precipitating cause identified. On admission, low bicarbonate level and high anion gap metabolic acidosis were observed in all patients. Hypocalcaemia was the commonest (82%) and hyperchloremia the rarest (15%) electrolyte disturbance observed on admission. The proportion of patients with most electrolyte disturbances peaked at 12 hours, after which they started to decline. At the time of admission 48.5% had renal failure and 9.1% had pre renal failure. This deranged renal function was transient as evidenced by gradual decrease in proportion of children with renal failure with treatment. More than half of the patients (60%) required insulin infusion less than 24 hours and 90% for less than 48 hours. As many as $2/3^{rd}$ of patients were discharged prior to 2 weeks. Patients with electrolyte disturbances persisting at 24 hours required insulin infusion for a significantly longer duration ($x^2=23.776$, $p<0.001$). However this did not result in a significant prolongation of hospital stay. It was observed that out of 33 patients 9 (27%) had a culture positive sepsis. There was a slight prolongation of the duration of insulin infusion and hospital stay in culture positive group, though this was not statistically significant .

CONCLUSION

The relative proportions of various metabolic derangements in children with DKA are described. Patients with electrolyte disturbances persisting at 24 hours required insulin infusion for a significantly longer duration. Sepsis resulted in mild prolongation of insulin infusion and hospital stay, though not statistically significant.

INTRODUCTION

Diabetes mellitus is metabolic syndrome characterized by hyperglycemia as a cardinal feature. Type 1 DM is due to immune depletion of β cells.

Diabetic ketoacidosis (DKA) results from absolute or relative deficiency of circulating insulin and the combined effects of increased levels of the counter regulatory hormones: glucagon, catecholamines, growth hormone and cortisol Absolute insulin deficiency presents in previously undiagnosed type 1 diabetes mellitus and patients on treatment who deliberately, inadequately or do not take insulin, especially the long-acting component of a basal-bolus regimen. Patients who are all on insulin pump can also develop DKA when insulin delivery fails for any reason. Relative insulin deficiency can occur when the concentrations of counter regulatory hormones by increase in response to stress in such conditions like trauma, sepsis, or diarrhoea and vomiting.[1,2]

In condition where there is low serum insulin and high counter regulatory hormones. There occurs an increased catabolic state with increased glucose production by the liver and kidney through glycogenolysis and gluconeogenesis. Impairment in peripheral glucose utilization results in hyperglycemia , increased lipolysis, hyperosmolality and and ketogenesis. This causes in ketonemia and metabolic acidosis. If hyperglycemia increases more than renal threshold (approximately 10 mmol/L [180 mg/dL]) it results in osmotic diuresis and obligatory loss of electrolytes, causing dehydration which is aggravated by vomiting. These changes also stimulate further stress hormone

production. This leads to worsening hyperglycemia, more severe insulin resistance and hyperketonemia. If this progression is not controlled with exogenous insulin, fluid and electrolyte therapy, it will cause fatal dehydration and metabolic acidosis. Ketoacidosis also aggravated by lactic acidosis caused from poor tissue perfusion and sepsis.

Classification of DKA[1]

	Mild	**Moderate**	**Severe**
Co2(mEq/L)	16-20	10-15	<10
pH(venous)	7.25-7.35	7.15-7.25	<7.15
Clinical	Oriented, alert and fatigued	Kussumaul breathing, oriented but sleepy and arousable	Kussumaul or depressed respiration. Sleepy to depressed sensorium to Coma

History

The first full description of diabetic ketoacidosis is described by Julius Dreschfeld. He was a German pathologist working in Manchester, United Kingdom. He described this condition in an 1886 lecture at the Royal College of Physicians in London, and explained reports by Adolph Kussmaul, describing the main ketones such as acetoacetate and β-hydroxybutyrate, and their chemical determination. The condition remained universally fatal until the discovery of insulin in the 1920s; by this discovery in 1930s, mortality had fallen to 29%, and by the 1950s it had become less than 10%. The entity of

cerebral edema due to DKA was described 1936 by a team of doctors from Philadelphia.

Since the 1950s numerous research studies were conducted for the ideal treatment for diabetic ketoacidosis. A significant proportion of these studies have been conducted at the University of Tennessee Health Science Center and Emory University School of Medicine. Treatment options studied have included such as high- or low-dose intravenous, intramuscular (e.g. the "Alberti regime") or subcutaneous insulin, need for a loading dose of insulin, phosphate supplementation and appropriateness of using bicarbonate therapy in moderate DKA. Various questions remain unanswered, such as whether bicarbonate administration in severe DKA makes any real difference to the clinical course, and whether an insulin loading dose is needed in adults.

The entity of ketosis-prone type 2 diabetes was first fully described in 1987 after several preceding case reports. It was initially thought to be a form of maturity onset diabetes of the young, and went through several other descriptive names (such as "idiopathic type 1 diabetes", "Flatbush diabetes", "atypical diabetes" and "type 1.5 diabetes") before the current terminology of "ketosis-prone type 2 diabetes" was adopted.

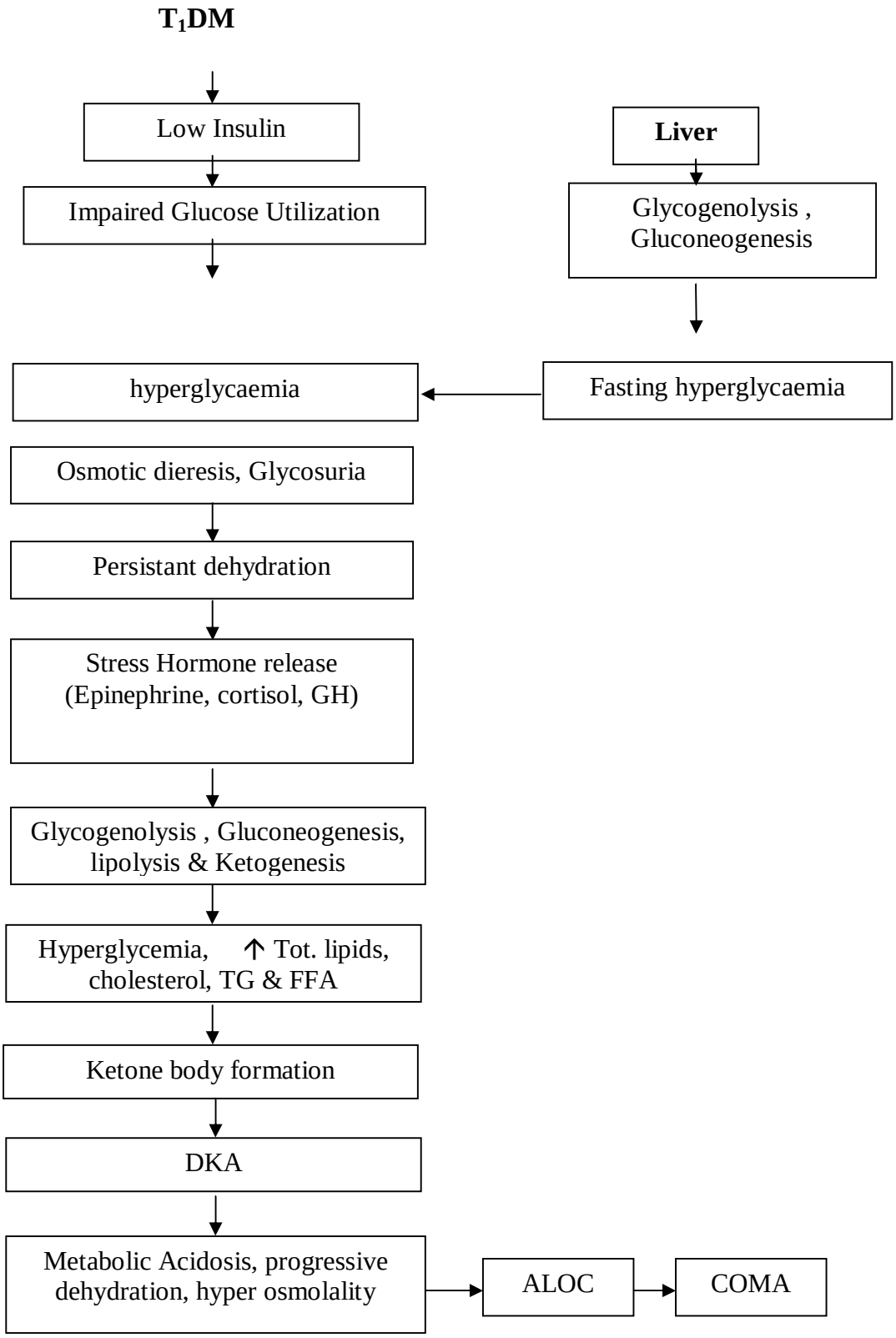
Epidemiology

Diabetic ketoacidosis and hyperosmolar hyperglycaemic state represent 2 extremes in the spectrum of decompensated diabetes. In Denmark, the annual incidence of DKA is approximately 12.6/100,000 which is higher in men than in women. Twelve percent of patients, usually those aged over 50 years, were diagnosed with type 2 diabetes, and overall mortality was 4%, mainly in patients aged over 70 years. In Sweden, 16% of children with new-onset diabetes presented with DKA; cerebral oedema occurred in 0.68% of cases. In Finland, a similar level of DKA in children presenting with type 1 diabetes was seen during the period 1992-2001; however, the overall frequency had generally decreased since 1982, with children aged under 2 years being those at highest risk of DKA at diagnosis. In Brazil, DKA occurred in 32.8% of patients at diagnosis of type 1 diabetes, mainly in children aged below 10 years, and more frequently in non-white than in white people. In the US, the annual incidence of DKA from population-based studies range from 4 to 8 episodes per 1,000 patient admissions with diabetes. The incidence of DKA increased in recent years. DKA accounting for about 136,510 hospitalisations in the US in 2006. The rate of hospital admissions for HHS is less than DKA and is <1% of all diabetic-related admissions. Decompensated diabetes causes a heavy burden in terms of economics and patient outcomes. In the US, DKA is accounts more than 500,000 hospital days per year and estimated annual direct medical expense and indirect costs of 2.4 billion USD. The mortality for

DKA started falling over recent years. Age-adjusted mortality for DKA dropped by 22% between 1980 and 2003.

Pathophysiology

Insulin deficiency causes increased secretion of counter regulatory hormones. This imbalance causes lipolysis, glycogenolysis, gluconogenisis and deceased peripheral utilisation of glucose which leads to hyperglycemia which leads to osmotic diuresis, polydipsea and polyuria . Dehydration and electrolyte loss in course of time cause impaired renal perfusion. Increased ketogenisis and lypolysis leads to ketoacidosis[15]


T1DM
Low Insulin
Impaired Glucose Utilization
Liver
Glycogenolysis , Gluconeogenesis
hyperglycaemia
Fasting hyperglycaemia
Osmotic dieresis, Glycosuria
Persistant dehydration
Stress Hormone release (Epinephrine, cortisol, GH)
Glycogenolysis , Gluconeogenesis, lipolysis & Ketogenesis
Hyperglycemia, ↑ Tot. lipids, cholesterol, TG & FFA
Ketone body formation
DKA
Metabolic Acidosis, progressive dehydration, hyper osmolality
ALOC
COMA

Electrolytes

1. Sodium[3]

Average sodium loss in DKA is 6 mEq/kg.

The following disturbances in sodium levels can occur -

(i) Hyponatremia

Pseudohyponatremia due to hyperlipidemia and hypoproteinemia,

Hyperglycemia induces movement of water out of the cells causes dilutional hyponatremia.[4,5]

Osmotic dieresis causes hypovolemic hyponatremia.

Insulin induced hyponatremia during the time of treatment.)

(ii) Hypernatremia

Pseudohypernatremia seen in hypoproteinemia.

Loss of water in osmotic dieresis is not replaced insufficiently can lead hypernatremia[6]

2. Potassium

Average potassium Loss in DKA is 5 mEq/kg

(i) Hypokalemia

Shift hypokalemia is due to insulin administration during the treatment

Gastrointestinal loss of potassium may associated with diarrheal states

Renal loss of potassium is common due to osmotic dieresis and hypomagnesemia.[7]

Hypokalemia can be caused by hyperglycemia.[8]

(ii) Hyperkalemia

Shift hyperkalemia associated with acidosis

Insulin deficiency and rhabdomyolysis, .

Reduced glomerular filtration of potassium due to acute and chronic kidney disease.[9]

c. Chloride [2]

Average Loss of chloride in DKA is 4 mEq/kg

Excessive replacement may leads to hyperchloremic acidosis.

d. Blood urea nitrogen and creatinine

Dehydration in the dka causes elevation both BUN and creatinin

Creatinine level elevated due to the presence of ketones

5. Magnesium

Hypomagnesemia

Pseudohypomagnesemia associated with hypoalbuminemia.

Shift hypomagnesemia caused by insulin administration.[10]

Poor dietary Magnesium intake

Gastrointestinal Magnesium losses caused by diarrhoea .

Increased renal Magnesium losses due to osmotic diuresis, glomerular hyperfiltration and recurrent metabolic acidosis. [11,12]

6. Phosphate

Total body losses phospherous in DKA average 3 mEq/kg .

Hypophosphatemia

In DKA hypophosphatemia is due to Osmotic diuresis and insulin administration. [12,13]

Primary hyperthyroidism may associated with diabetes mellitus also leads to hypophosphatemia in hyperglycaemic crisis

7. Calcium

In type I diabetes may associated with autoimmune hyperparathyroidism that can cause hypercalcemia.[14]

Hypocalcemia

Pseudohypocalcemia is due to hypoalbuminemia.

Hypocalcemia presented in acute renal failure due to accompanying hyperphosphatemia.

Advanced chronic renal insufficiency due to hyperphosphatemia and low levels of vitamin D.

RISK FACTORS[2]

- ✓ Undiagnosed type I DM
- ✓ Children with previous episodes of DKA or poor metabolic control
- ✓ Peripubertal and adolescent female
- ✓ Children with pre existing disease such as psychiatric disorders, including those with eating disorders
- ✓ Children with difficult or unstable family circumstances
- ✓ Children who fails to take insulin
- ✓ Children with minimal access to medical services
- ✓ Insulin pump therapy - only rapid or short-acting insulin is used in pumps, interruption of insulin delivery for any reason rapidly leads to insulin deficiency[16]

CLINICAL FEATURES [2]

- Abdominal discomfort
- Nausea
- vomiting
- Kussmaul breathing
- Fruity odor
- Dehydration
- Cognitive dysfunction

Diagnosis of Diabetic Ketoacidosis :[2]

DKA – hyper glycaemia that is blood glucose > 11.1mmol/Lt (or) 200 mg/dl with a venous PH of < 7.3 (or) HCO3 < 15mmo/Lt, associated with ketonuria, glycosuria &ketonaemia.[15]

Emergency Assessment

Perform a rapid clinical evaluation to confirm the diagnosis and to determine the cause also look for foci of infection. Weighing the patient is important because this weight should be used for calculations and do not use the weight from a previous hospital record.

Assess clinical severity of dehydration.

Clinical assessment of dehydration is inaccurate, imprecise, and generally shows only fair to moderate agreement among examiners. It should be assess based on a combining with physical signs of dehydration. Three most useful signs for assessing dehydration and acidosis in children with 5% dehydration are Prolonged capillary refill time (normal capillary refill is ≤ 2 seconds)[16]

Hyperpnea

Abnormal skin turgor

Other signs of assessing the degree of dehydration include:

Dry mucus membranes

Absent tears

Sunken eyes

Cool extremities

Weak pulses

More signs will be associated with more severe dehydration.

≥ 10% dehydration is suggested in presence of weak or impalpable peripheral pulses, hypotension and oliguria.

Assess level of consciousness (Glasgow coma scale [GCS] – [17]

Best eye response	**Best verbal response**	**(Nonverbal Children)**	**Best motor response**
1. No eye opening	1. No verbal response	1. No response	1. No motor response
2. Eyes open to pain	2. No words, only incomprehensible sounds; moaning	2. Inconsolable, irritable, restless, cries	2. Extension to pain (decerebrate posture)
3. Eyes open to verbal command	3. Words, but incoherent	3. Inconsistently consolable and moans; makes vocal sounds	3. Flexion to pain (decorticate posture)
4. Eyes open spontaneously	4. Confused, disoriented conversation	4. Consolable when crying and interacts inappropriately	4. Withdrawal from pain
	5. Orientated, normal conversation	5. Smiles, oriented to sound, follows objects and interacts	5. Localizes pain
			6. Obeys commands

Biochemical assessment[2]

- Collect blood samples for laboratory investigations such as
- Serum or plasma glucose
- Blood urea nitrogen creatinine
- Electrolytes (including sodium, potassium, chloride, bicarbonate or total carbon dioxide)
- Calcium
- Magnesium
- Phosphorus
- Venous (or arterial in critically ill patient) pH, pCO_2
- HbA1c (it can differentiate diabetes mellitus from other causes)

Complete blood count including haemoglobin and hematocrite (in an elevated total leukocyte count in response to stress is characteristic of DKA and its not necessarily indicative of infection)

Perform a urinalysis for ketones.

Measurement of blood ß-hydroxybutyrate concentration, if available, is useful to confirm ketoacidosis and may be used to monitor the response to treatment.[18,19,20] Collect specimens for cultures such as blood, urine and throat in the view of infection.

ECG (If laboratory result of serum potassium is delayed, perform an electrocardiogram (ECG) for baseline evaluation of potassium status)

Treatment of Diabetic Ketoacidosis :

This is the most severe and fatal complication of Type I Diabetes.

Goals of treatment

- Prevent the development of cerebral edema.
- Slow correction of dehydration and acidosis

1. Correction of fluid deficits and shock correction.
2. Dehydration correction and maintain the circulation .
3. Stop ketoacid production – Insulin Therapy
4. Evaluation and treatment of precipitating cause.
5. Close monitoring for complications such as cerebral edema, hypoglycemia and hypokalemia[15]

I. Fluid and Salt Management

- Anion gap= Na –(cl+HCO3)
- Normal = 12 +/- 2 mmol/L
- In dka it will be 20-30 mmol/L[15]
- Corrected Na= measured Na+ 2([plasma glucose-5.6]/5.6) mmol/L
- Effective osmolality = (mOsm / kg)2 *(Na+K)+ glucose(mmol/L)
- Patient with DKA has deficit in ECF volume about 5-10%
- In severe DKA 7-10% fluid correction is required
- In moderate dka 5-7% of fluid correction is required

Serum sodium correction using the above mentioned formula is helpful to maintain appropriate Na in serum because lab values of sodium will show

dialutional hyponatremia in hyperglycaemia and low sodium content in elevated lipid fraction[10]

Principles of water and salt replacement[15]

- Salt and water deficit should be corrected
- For patient without shock + with severe volume depletion should be treated with 0.9% saline and restore the peripheral circulation
- For patient with shock 20ml / kg boluses infused rapidly fluid either .9% saline or Ringer lactate.
- Subsequently deficit replacement can be done with .9% saline or ringer lactate over 4-6 hrs
- Additional assessment of dehydration and effective osmolality calculation help in guiding the fluid therapy
- Urinary sodium loss calculated in replacement therapy.
- Large use 0.9% saline may lead hyper chlorimic metabolic acidosis

II. Dehydration correction → Rehydration Fluid:

Deficit correction + maintenance fluid

1. If the child presents with shock a deficit of 100 ml/kg is assumed (10% dehydration)
2. If the child is not in shock then deficit of 85 ml/kg (8.5% dehydration) is assumed.

FOR EXAMPLE :

Maintenance fluid, for example for a 20 kg child presented with shock & DKA

Shock correction →10 ml/kg (200ml) over 1 hour

Maintenance fluid for 48 hrs = 1500 x 2 = 3000 ml

Deficit 100 ml/kg = 2000 ml

Initial fluid = 0.9% NS

Total fluid = Deficit + maintenance fluid for 48 hrs – fluid bolus (during 1^{st}hr)

= 3000 + 2000 – 200 = 4800 ml over 47 hrs

Total fluid intake is should be < $4L/m^2$/24 hr

III. Insulin Therapy :

Insulin infusion at the rate of 0.05-0.1 U/kg/hr after correction of shock

Insulin should be given through by a separate Infusion pump not with rehydration fluid or ionotropes.

When the blood glucose level reach below 250 mg/dl change the Rehydration fluid from 0.9 normal saline to D ½ NS.

Usually hyperglycemia corrects faster than acidosis. So the rehydration fluid should be changed to 7.5%, 10% or 12.5% dextrose according to the blood glucose level and Insulin infusion should be continued till the acidosis gets corrected.

Start subcutaneous Insulin therapy once acidosis fully resolved and once the child starts taking oral feeds. Continue insulin infusion for an hour after giving 1st dose of subcutaneous regular Insulin.

Potassium Administration[2] :

Total body deficit of potassium in DKA is 3-6 mmol/ kg. replacement therapy is required regardless of the serum potassium values. In hypokalema initial potassium replacement starts with initial rapid volume expansion at a concentration of 20 mmol /L. potassium replacement in infusion will be 40 mmol/l. potassium replacement should be continue throughout the treatment. Maximum dose can be given upto 0.5 mmol / kg/ L. If hypokalemia persist even at maximum dose of potassium then the rate of insulin infusion can be reduced.

Bicarbonate Administration

Bicarbonate infusion indicated in below mentioned condition, bicarbonate correction can be give 1-2 mmol/ kg slowly over 1 – 2 hrs in case of

1. Severe acidosisin Ph -< 6.9
2. Impending Cardio Vascular Collapse
3. Imminent arrest
4. Acidosis may interfere the action of ionotropes such as epinephrine

Complication of bicarbonate therapy

a) Hypoglycemia
b) Hypokalemia
c) Cerebral edema
d) Inadequate rehydration
e) Hyperchlorimic acidosis

Monitoring

1. Vital signs monitoring Hourly
2. Neurological sings monitoring 1 – 2 hourly.
3. Input & Output monitoring hourly.
4. Blood sugar, electrolyte, pH, HCO3 – monitoring initially
   1 – 2 hourly then every 4th hourly
5. Calcium, Phosphate and Magnesium levels every 12th hourly.
6. HbA1C, Lipid profile, Insulin auto antibodies.
7. Sepsis screening.
8. X rays.

Complications of DKA[2]

1)Hypoglycaemia

This one of the complication occurs with excessive high-dose insulin therapy. It can be prevented by strict following of current treatment protocols with frequent monitoring of blood sugar and use of glucose-containing IV fluids.

2)Hypokalaemia

This is common complication can occur with excessive high-dose insulin therapy and bicarbonate therapy. It can be prevented by following current treatment protocols with frequent monitoring of potassium levels and appropriate replacement

3) Non-anion gap hyperchloraemic acidosis

This occurs due to urinary loss of ketoanions needed for bicarbonate regeneration, and also increased re absorption of chloride secondary to intensive administration of chloride-containing fluids. This acidosis usually resolves and should not affect the treatment.

4) Cerebral oedema

This is major cause of mortality in DKA. This occurs in 0.7% to 10% of children with diabetic ketoacidosis (DKA) and is rare in adults with DKA and in patients with hyperosmolar hyperglycaemic state (HHS).

Diagnostic criteria

Abnormal motor or verbal response to pain

Decerebrate or decorticate posture

Cranial nerve palsy (especially 3,4,6)

Abnormal neurogenic respiratory pattern(grunting, tachypnea, cheyne stokes respiration, apneusis)

Major criteria

Age in appropriate incontinence of urine

Altered mental status

Sustained heart deceleration

Minor criteria

Vomiting

Head ach

Lethargy age< 5 years

Diastolic BP- > 90mm of Hg

One diagnostic criterion, two major criteria or one major and two minor criteria have sensitivity 92% and false positive 4%.[2]

Investigation

CT Brain- to rule out other causes of intracerebral complication for deterioration.

Treatment

Mannitol iv 0.5- 1 gm / kg stat dose over 20minutes and if no improvement with in 30minutes to 2 hours same dose can be repeated.

3% saline 5- 10 ml /kg over 30 minutes . Used as a alternative to Mannitol or no improvement with Mannitol.

Intubation and mechanical ventilation may required if respiratory failure happened.

Mortality is very high.

If above mentioned symptoms are present child should be treated with Mannitol infusion and mechanical ventilation . condition can be Prevented by avoidance of over- hydration and by maintaining the glucose level at 8.3 to

11.1 mmol/L (150 to 200 mg/dL) in DKA and 13.9 to 16.7 mmol/L (250 to 300 mg/dL) in HHS.

5) Acute respiratory distress syndrome (ARDS)

Reduction in colloid osmotic pressure by treatment may lead to accumulation of water in the lungs and decreased lung compliance and possible cause of hypoxaemia in diabetic ketoacidosis. The management includes the monitoring of blood oxygen levels with pulse oximetry and lowering the fluid intake with addition of colloid replacement

6) Hyperkalemia

7) Sepsis[21]

8) Rhabdomyolysis

9) Acute renal failure[22]

Differential diagnosis

Asthma

Pneumonia

Acute abdomen

Gastroenteritis

Salicylate toxicity

Prevention[2]

For preventing diabetic ketoacidosis and other diabetes complications.

- Make healthy eating and physical activity part of your daily routine. Take appropriate dose of insulin as advised by physician
- Monitor blood sugar level regularly .
- Check and record blood sugar level at least three to four times a day — if child ill or under stress. Careful monitoring is the only way to make sure your blood sugar level remains within your target range.
- Adjust insulin dosage as needed as advised by doctor or diabetes educator for relation to your blood sugar level, If patient is ill and other factors like stressful condition can cause rise blood sugar level.
- Check ketone level. When child is ill or under stress, if excess ketones with an over-the-counter urine ketones test kit. If ketone level is moderate or high, advice the patient to get admitted. If you have low levels of ketones, you may need to take more insulin.

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REVIEW OF LITERATURE

In a study conducted by Kanwal S K, Bando A, Kumar V showed that mean age 7.4+/- 3.9.27males and 28 females were included in study.56.4 % were new onset diabetic patient . DKA presenting symptoms were polyuria and polydipsia (54.5%), persistent vomiting (52.7%), altered sensorium (50%)abdominal pain (47.3%). Most of the patient had dehydration at admission and 25% were having severe dehydration. Electrolyte imbalances such as hypernatremia (20%) and hypokalemia (14.5%) were observed in this study. Renal failure was found in 7.2% of patients and cerebral edema in 14.5 % of patients. Renal failure, cerebral edema and sepsis were the reasons for adverse outcome.[17]

Ogbera AO, Awobusuyi J, Unachukwu C,Fasanmade O conducted a study named clinical features predictive factors and outcome of hyperglycaemic emergencies in developing country in a back ground of death is seen in Nigeria due to hyperglycemic emergencies..This study showed that DKA is more than HHS.DKA is present in type 1 diabetes (81%) than type 2 diabetes.. In DKA patients hypokalemia was present in 37%. 57% had elevated urea and 19% had hyponatremia in DKA patients. Predictive factors for mortality in this community were sepsis, previously undetected diabetes mellitus and hypokalemia.[23]

In a study conducted by Andrew E Edo showed that showed that 55.2 % patients were first time diagnosis of diabetes mellitus. Precipitating factors for this were poor drug compliance (27.4%), malaria(14%), urinary tract infection

(11.9%) and un identifiable (34.5%). Common metabolic derangements were hypokalemia(25%) and hyponatremia (36.9%).[24]

In a study conducted by Moulik , nirmalya roy MD, Jayasree M. MD, Singhi, Sunit MD, Bhalla, Anil kumar PhD, Attri, Savitha PhD to assess the nutritional status of patient presenting with DKA and correlate it with incidence of complication at presentation and those encountered during the course of illness. In this study observed that33.3% were malnourished, 63.3% were having hypoalbuminemia. Incidence and severity of therapy related hypokalemia (100% vs 72.7%; p= .05) and hypoglycemia (63.6 vs 13.6 %) were significantly high in malnourished children. During the time of admission serum potassium was similar in both groups. Incidence of renal failure, cerebral edema and sepsis were similar in both groups. Incidence of treatment related hypokalemia and hypoglycemia were significantly higher in malnourished children.[25]

In a study conducted by Varadarajan Poovazhagi regarding risk factors for mortality in children with DKA from developing countries observed that renal failure, shock, sepsis and cerebral edema are the major risk factors for mortality. Cerebral edema was significantly associated with failure of sodium to rise with therapy.[26]

In a study conducted by C.F. Otieno, J.K. Kamiya, P.K.Mbugua, A.A. Amayo and S. O. Mclgeyo about clinco- laboratory predictor s of outcome of patients with DKA observed that 29.8% died ,all of them died less than 48 hours and all of them had altered level of consciousness . Altered level of

consciousness was associated with elevated renal parameter and very severe acidosis.[27]

Study conducted by Moses S elisaf, Agathoklis. A, Tsatsoulis, Kostas C. Siamopoulos, Kostas C. Katopodis observed out 40 patients 22 patient s were having pure metabolic acidosis . 7 were combined hyper chloremic metabolic acidosis 3 were having respiratory alkalosis and 9 were having combined metabolic alkalosis. Hydration status as evidenced ratio of urea and creatinine seems to play important role in the development of mixed acid base disorder. Hyper chloremic acidosis developed in better hydration status patients. Patients with DKA with pneumonia showed respiratory alkalosis.[16]

Study conducted by George Liamis, Evangelos Liberopoulos, Fotios Barkas, Moses elisaf showed that diabetic patients frequently had metabolic disorder and this will be higher in DKA and HHS. These patients having depleted level of potassium, magnesium and phosphate. Both hyper and hypo natremia reflecting the coexisting hyperglycemia. Diabetes mellitus with renal failure leads to hyperkalemia during emergencies. In DKA hypercalcemia was present in this population.[15]

AIM AND OBJECTIVE OF THE STUDY

OBJECTIVES:

Primary Objective:

To study the metabolic derangements in DKA in 1st 48 hours of admission.

Secondary Objective:

To determine its relation with duration of insulin infusion and hospital stay.

To determine the relation between sepsis with duration of insulin infusion rand hospital stay.

STUDY JUSTIFICATION

1. DKA is the most common presentation of children with type 1 diabetes mellitus.
2. Most of the previous studies in DKA focused on precipitating factors and its management.
3. No study was done on various metabolic derangements occurring in DKA which influence its prognosis.
4. With the average of 24 cases per year for the past 10 years in ICH, it would be a fitting place to conduct a study on DKA.
5. This study will bring out metabolic derangement in DKA.
6. This study will help to predict the average hospital stay and insulin infusion requirement for a patient with DKA.
7. This study will bring out the relationship between sepsis and duration of insulin infusion and length of hospital stay

MATERIALS & METHODS

Study design:

Descriptive study

Study place:

Pediatric intensive care unit

Institute of Child Health and Hospital for Children, Egmore, Chennai-8

Madras Medical college- Chennai

Study period:

January 2015 – September 2015

Study population:

I**NCLUSION CRITERIA:**

Children with DKA who are admitted in paediatric intensive care unit of ICH & HC.

EXCLUSION CRITERIA:

Children admitted with DKA are partially treated in outside hospitals for DKA.

SAMPLE SIZE:

Hospital incidence is 7%. For 5% level of significance for 90 % power sample size needed 56. And for 80 % power sample size needed is 33.

MANOUEVRE

Children were enrolled on the basis of inclusion criteria after obtaining written informed consent from the parents / guardians. Diagnosis of DKA made based on the standard definition.[2]

The following details were noted in the data collection form-

Age, sex and presence of pre existing diabetes. If found to have pre-existent diabetes, duration of diabetes, insulin requirement, glycosylated haemoglobin (HbA1C) and interval between DKA and last available HbA1C were noted.

Family history of diabetes was elicited. Presence of any identifiable precipitating cause like infection, stress or insufficient intake were noted.

Height was measured using stadiometer for children >2 years and recumbent length measured using infantometer for children <2 years using standard techniques. Weight of the patient was measured by electronic weighing scale with a least count of 50 gm with the child wearing light clothing.

Body mass index calculated by using standard formula- weight in kg /height in m2. [9] Anthropometric measures were interpreted using WHO chart for < 5years age and IAP chart for children > 5 years of age and classified accordingly.

5 ml of venous blood was drawn for estimation of urea, creatinine, electrolytes namely sodium and potassium. Serum sodium and potassium were checked by Ion Selective Electrode method-as per modified NCCLS

protocol. Blood urea and Serum creatinine evaluated automated chemistry analyzer.

Arterial blood was drawn in heparinised syringe for blood gas analysis. Acidosis, Chloride, bicarbonate and ionised calcium were measured by ABG machine, using Ion Selective Electrode method. ABG was interpreted as presence or absence of acidosis and type of acidosis present.

ABG Machine

Automated chemistry analyzer

Ion selective electrode auto analyzer for Na and K

The above said investigations were done at the time initiation of treatment, 12hrs, 24 hrs, 36 hrs and 48 hrs. All the children admitted were treated as per standard DKA protocol. All DKA children were monitored using the chart given below.[28]

Date & Time	HR	RR	BP	Perfusion	GCS	blood sugar	corrected Na	Insulin infusion	IVF	Remarks

For children who recovered or died before 48 hours, investigations were done only till that time. The time of stopping insulin infusion was noted for all patients. The clinical outcome of child and duration hospital stay were also noted.

Case Definitions

DKA

Hyperglycemia that is blood glucose > 11.1mmol/ lt OR 200 mg / dl with a venous PH of < 7.3 OR HCO3 < 15 mmol /lt associated with glycosuria, ketonuria and ketonaemia[2]

Sodium

Normal values Child-138 -145 Meq /L,[29]

Infants- 139- 146 Meq/ L[29]

Sodium values below and above the mentioned were classified as hypo and hyper natremia respectively.

Potassium

Normal value

2-12 months – 3.5- 6 Meq/L[29]

>12 months- 3.5-5 Meq/ L[29]

Potassium values below and above the mentioned were classified as hypo and hyperkalemia respectively.

CHLORIDE

Normal value- 80-110 mg /dl[29]

Chloride values below and above the mentioned were classified as hypo and hyperchloremia respectively.

BICARBONATE

Normal bicarbonate level- 20 -26 Meq[29]

Bicarbonate values above and below the mentioned were classified as alkalosis and acidosis respectively

CALCIUM

Normal value- 4.4-4.8 mg /d

Ionised Calcium values below and above the mentioned were classified as hypo and hyper calcemia respectively

ACIDOSIS [29]

Normal ph blood is 7.35-7.45

If ph < 7.35 – acidosis

>7.45 is alkalosis

HIGH ANION GAP METABOLIC ACIDOSIS

pH should be less than 7.35 and anion gap should be more than 11

NORMAL ANION GAP METABOLIC ACIDOSIS

pH should less than 7.35 and anion gap should be less than 11 [16]

RENAL FUNCTION TESTS

Urea

Normal value for infant and child:10.7-39 mg / dl

Blood urea interpreted as normal at above mentioned range and more than that considered as abnormal

Creatinine

Normal for child: 0.3- 0.7 mg / dl

Serum creatinine interpreted as normal at above mentioned range and more than that considered as abnormal

Interpretation of RFT

Divided in to 3 groups

1) Pre renal failure- only urea is elevated
2) Renal failure- both urea and creatinine are elevated
3) Normal – both urea and creatinine are in normal limit

Statistical Methods

Collected data entered in the Microsoft excel sheet. Data analysis done by SPSS software Version 20.

Continuous variables were categorised as either normal or abnormal and the patients in either category were reported as proportion. Duration of insulin infusion and duration of hospital stay in various categories were analysed using box and whisker plot

CONFLICT OF INTEREST : NIL

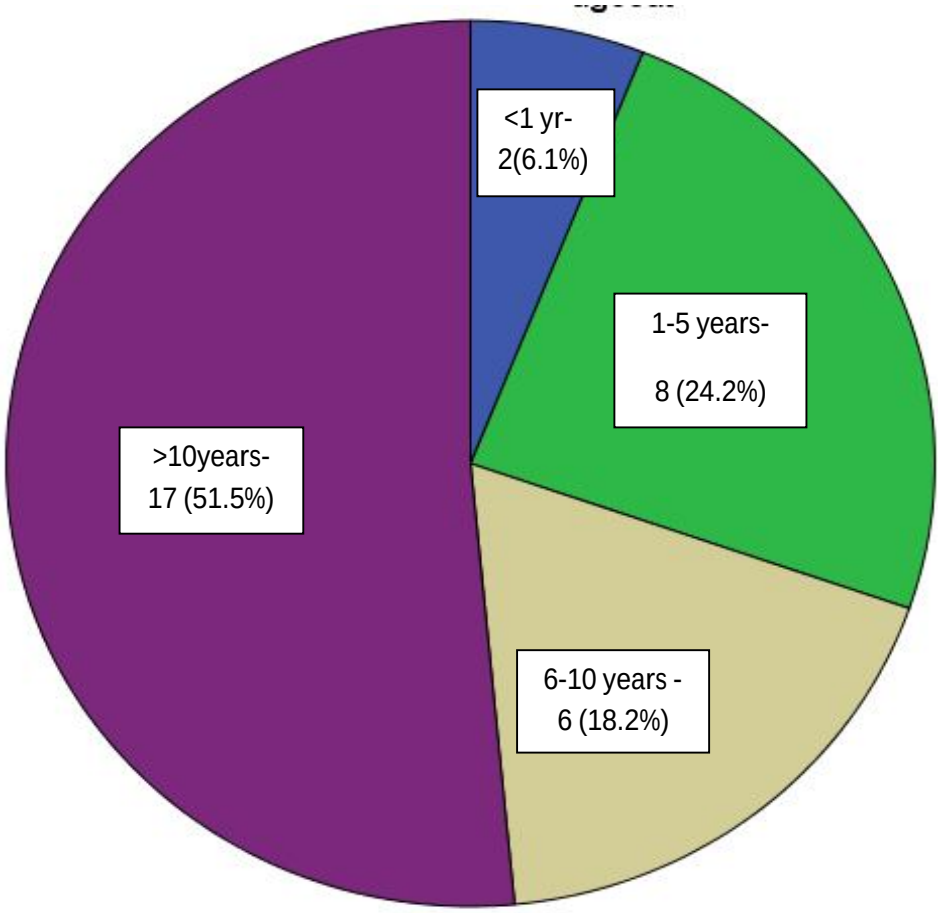
FINANCIAL SUPPORT : NIL

ETHICAL COMMITTEE CLEARANCE: Obtained

RESULTS

Totally 33 patients were treated in our hospital PICU during the study period and were included in the study.

AGE CATEGORY

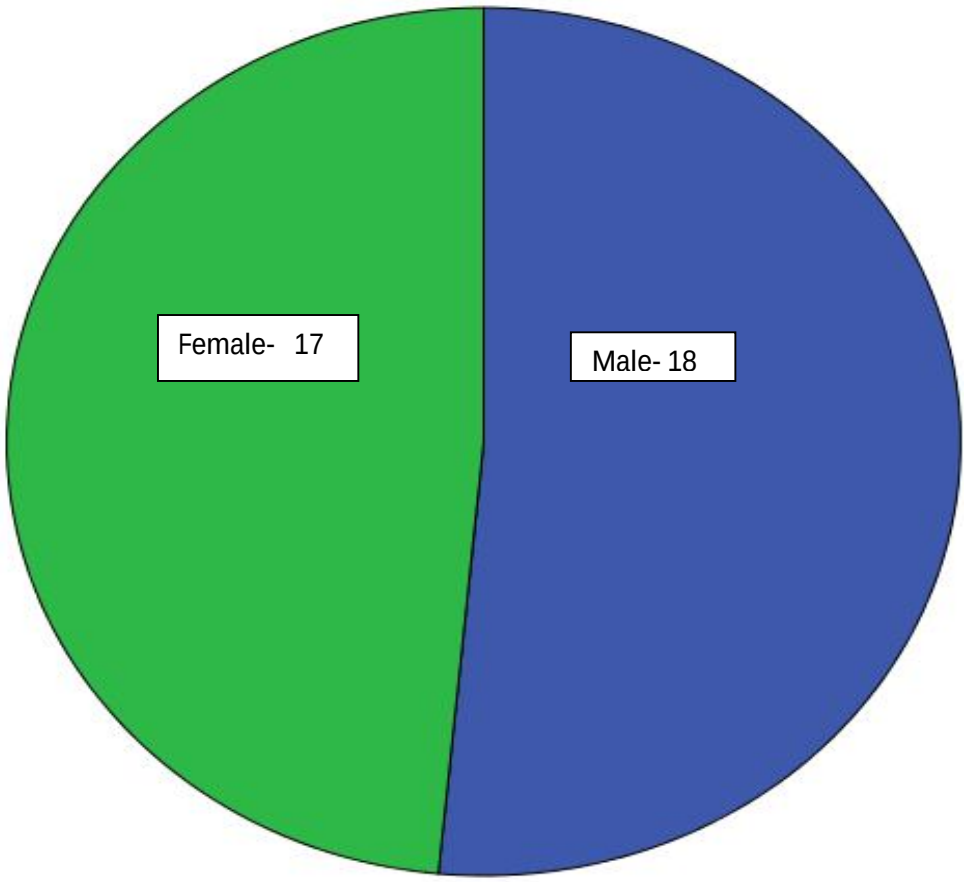


Almost half of the patients were more than 10 years (51.5%) of age and least common age group was infants (6.1%)

SEX RATIO

Calculated as male female ratio

1. Male
2. Female



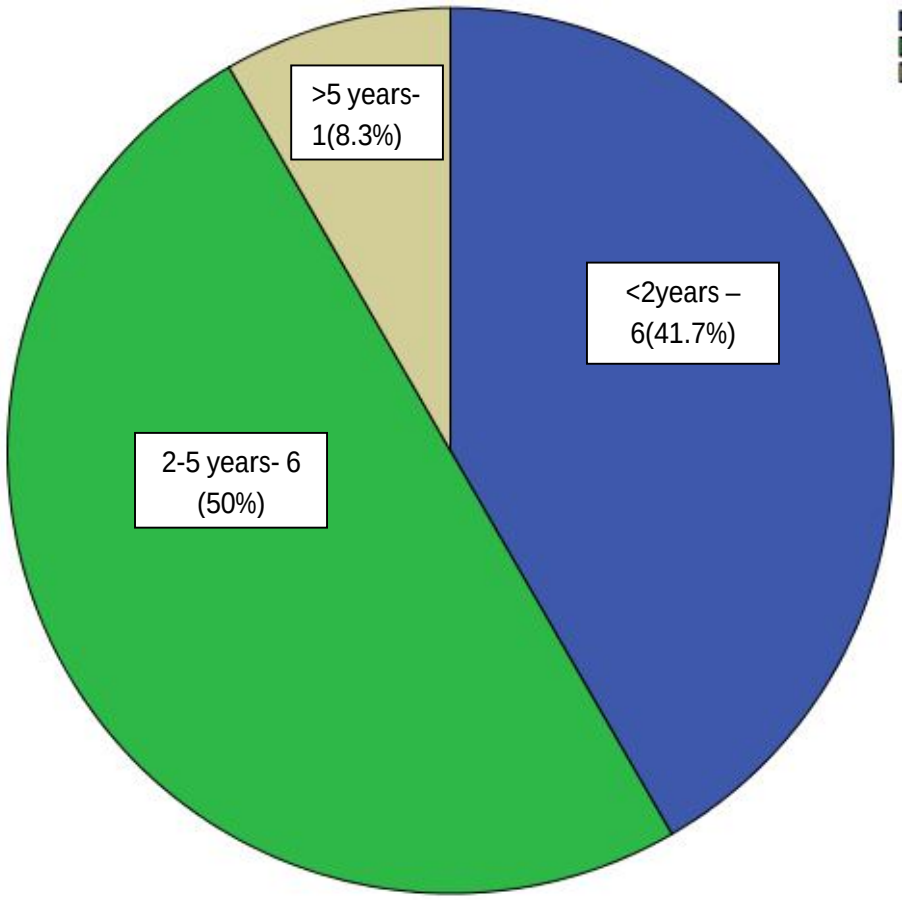
Number of males (18)and female(17) were almost same. Male female ratio in this study was 1.06:1

PRE EXISTING DIABETES

	Number	Percentage
Pre existing diabetes	12	36.4
New onset diabetes	21	63.6
Total	33	100

36.4% of children with DKA had pre existing diabetes while the rest 63.6% were new onset DKAs

DURATION OF DIABETES MELLITUS IN PRE EXISTING PATIENTS



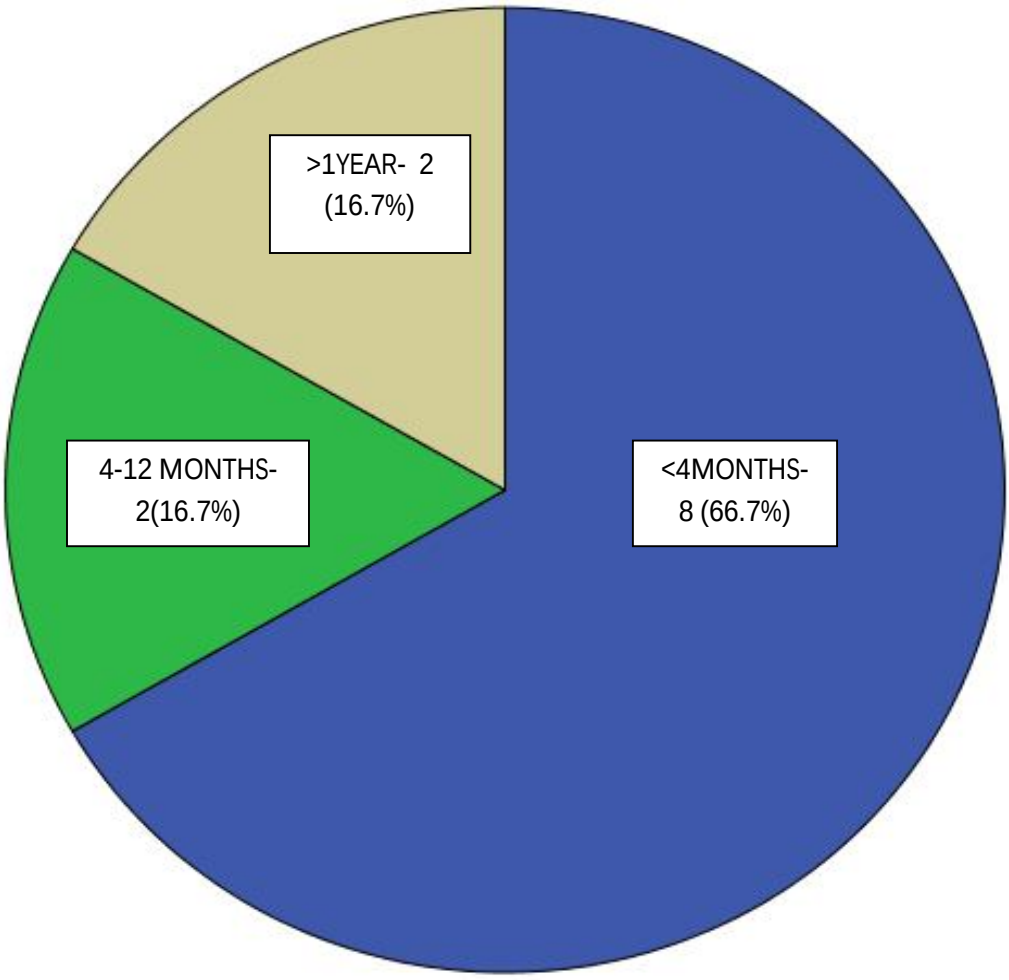
Out of 12 children with pre existing diabetes half of them were diabetics for 2-5 years and 41% were diabetics for < 2years. Only 1 case had diabetes for more than 5 years.

PRECEDING HbA1C STATUS IN PRE EXISTING DIABETIC GROUP

HbA1C	Number	percentage
7.5- 9	5	41.7
>9	7	58.3
Total	12	100

None of the children with pre existent diabetics who presented DKA had optimal glycemic control as evidenced by HbA1C levels less than 7.5. 42%had sub optimal control[2] (HbA1C 7.5-9) while 58% had poor control (HbA1C more than 100).

PRECEDING HbA1C GAP IN PRE EXISTANT DIABETICS



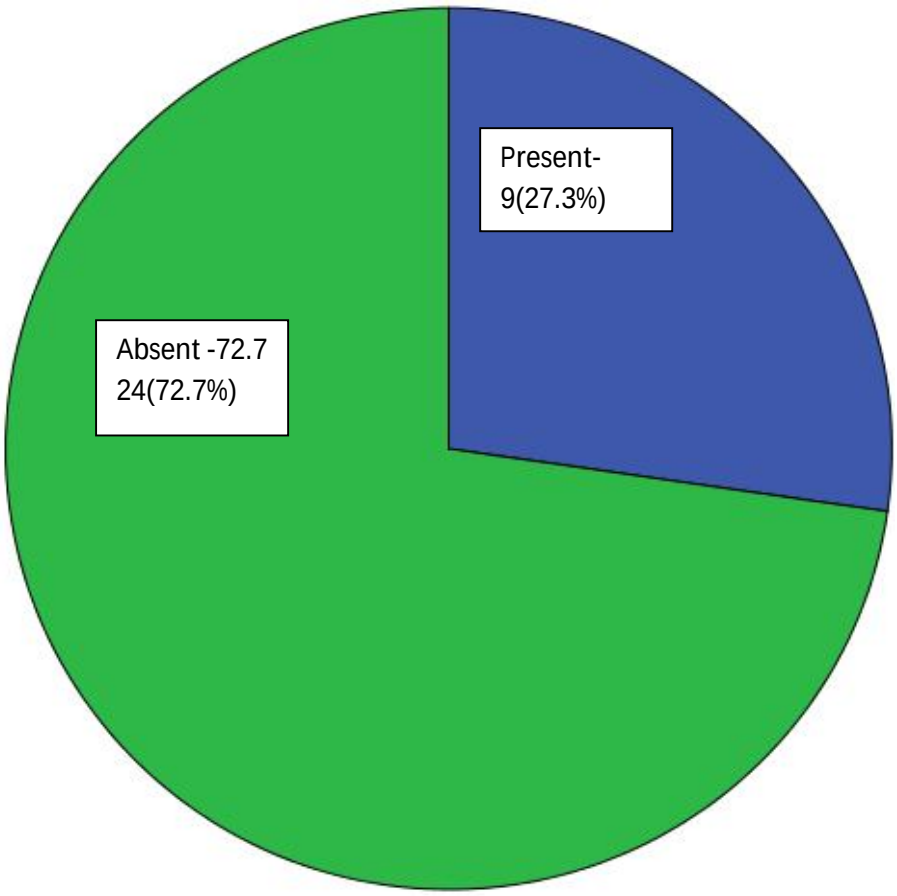
Almost 2/3 of them (66.7%) had their HbA1C estimated with in preceding 4 months, while rest had done between 4-12 months (16.7%) and > 1year (16.7%)

INSULIN DOSE IN PRE EXSITING DIABETICS PRIOR TO DKA ONSET

Insulin dose(u/kg/day)	Number	Percentage
0.5-1	4	33.3
1-1.5	6	50
>1.5	2	16.7
	12	100

Half of the patient with pre existing diabetes mellitus required 1-1.5 u/kg/day of insulin, while only 33% were on < 1 u/kg/day of insulin. A small fraction 16% of patients required more than 1.5 u/kg/ day.

FAMILY HISTORY OF DIABETES MELLITUS



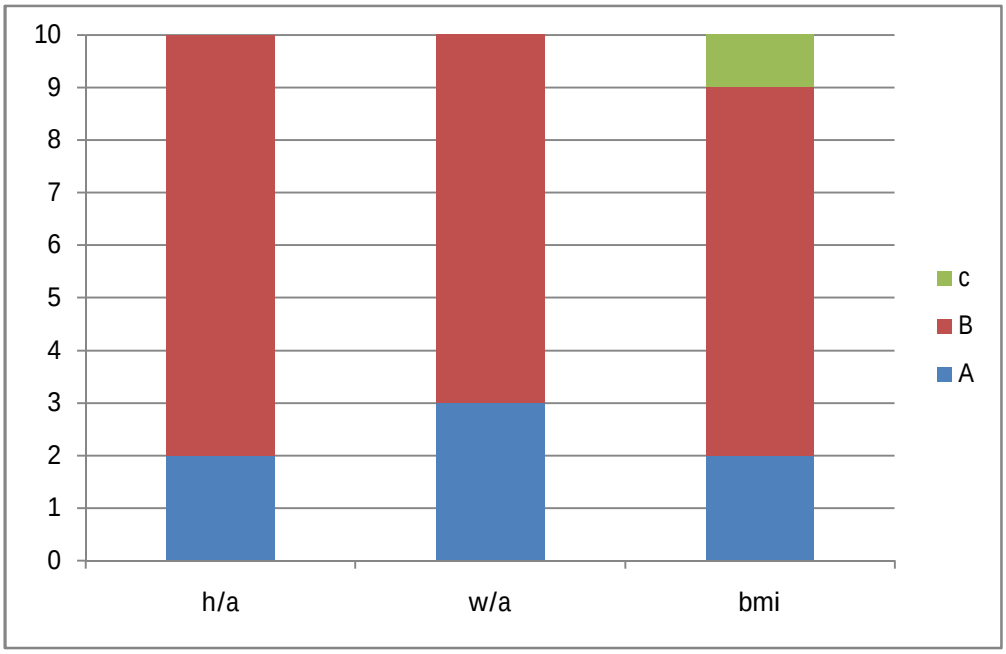
Positive family history was present in 27% of cases only.

PRECIPITATING CAUSE OF DKA

	Precipitating factor	number	Percentage
1	Infection	14	42.4
2	Insufficient insulin intake	3	9.1
3	Stress	0	0
4	Unknown	16	48.5
	Total	33	100

In this study in majority of the patient s (48.5%) precipitating cause is unknown. 14 patients(42.4%) were having some infection. 3 patients(9.1%) were having insufficient insulin intake.

ANTHROPOMETRY OF PATIENT <5 YEARS IN DKA



H/A **W/A** **BMI/ A**

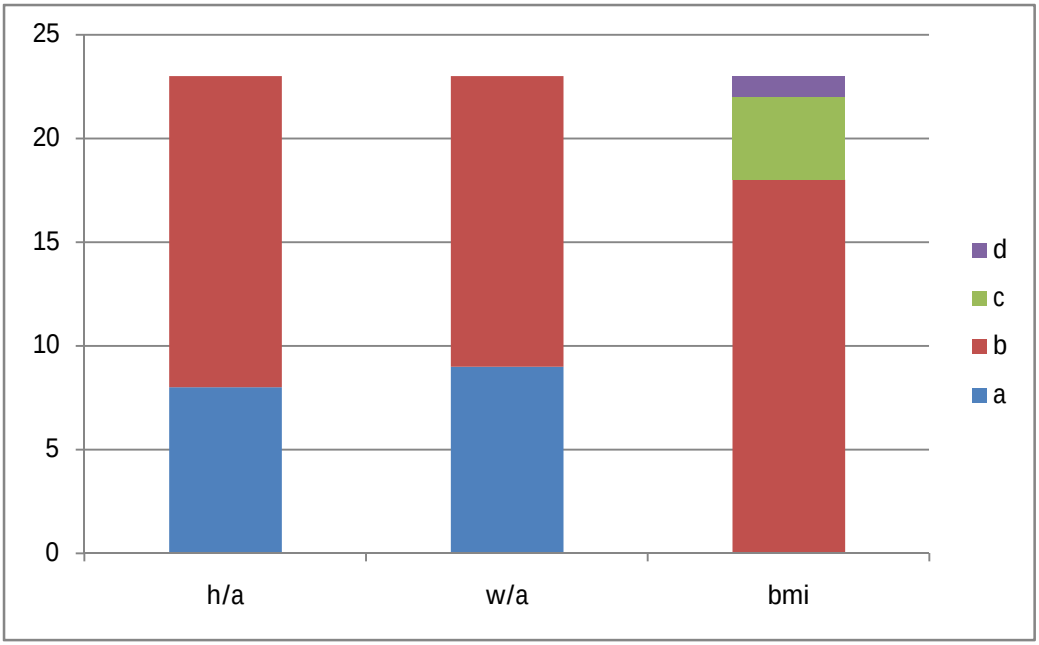
A) Short for age A) Under weight A) Under weight

B) Normal for age B) Normal B) Normal

C) Tall for age C) Risk of overweight

While analysing the anthropometric data of children less than 5 years, it was found that 20% had short stature, 30% were having under weight as per weight for age and 20% under weight as per BMI while 10% of children were at risk of overweight as per BMI. The remaining children had normal anthropometric measurements.

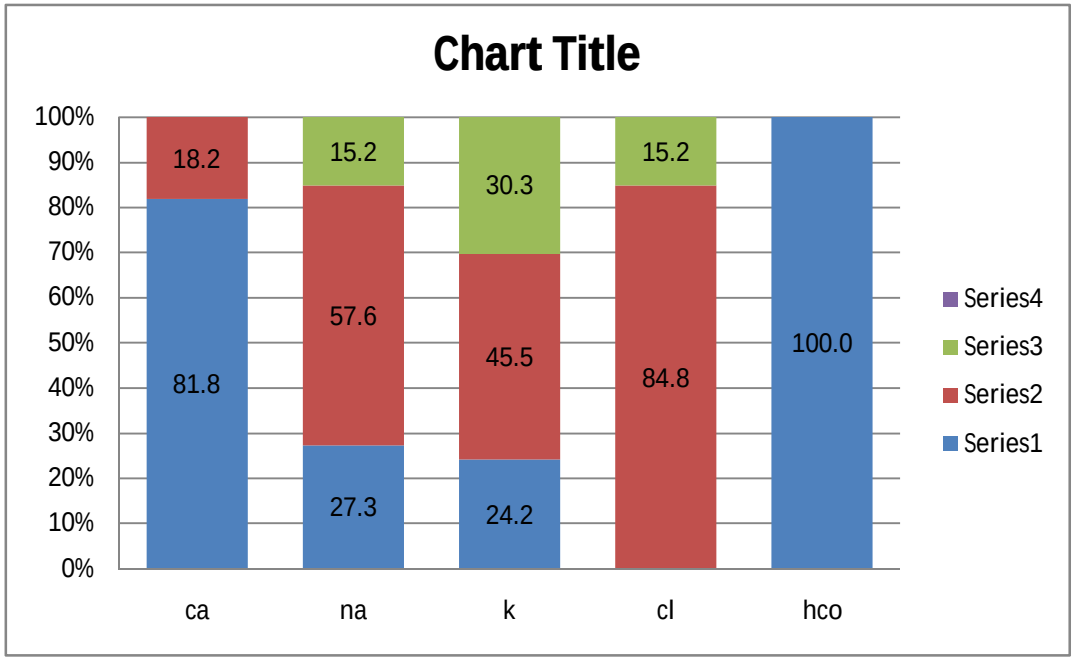
ANTHROPOMETRY OF PATIENT >5 YEARS IN DKA



H/A	W/A	BMI/ A
A) Short for age	A) Under weight	A) Under weight
B) Normal for age	B) Normal	B) Normal
C) Tall for age		C) Risk of overweight
		D) Obese

While analysing the anthropometric data of children more than 5 years, it was found that 34.7% had short stature, 39.1% were having under weight as per weight for age and no one belong to underweight while 17% of children were at risk of overweight and 3% were at obesity as per BMI. The remaining children had normal anthropometric measurements.

ELECTROLYTE IMBALANCES AT ADMISSION



Series 1 – less than normal

Series 2- normal

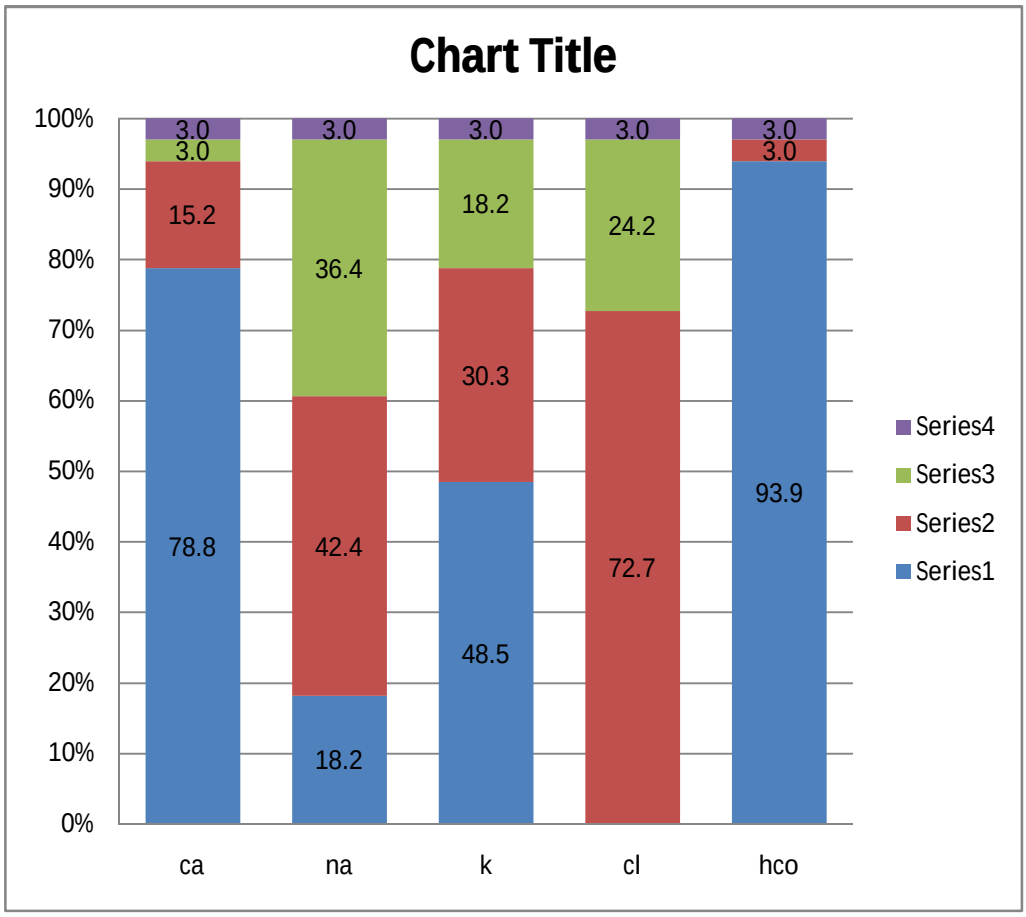
Series 3- more than normal

Series 4-not taken due to corrected the acidosis

In this study during the time of admission patients were having

1) Calcium-81.8% had hypocalcimia and18.2% has normal value
2) Sodium- 27.3% had hyponatremia,57.6% were in normal range and 15.2% had hypernatremia
3) Potassium-24.2% had hypokalemia, 45.5% had normal range and 30.3% were in hyperkalemia
4) Chloride- 84.4% had normal range and 15.2% had hyperchlorimia
5) Bicarbonate- 100% were in acidotic range

ELECTROLYTE IMBALANCES AT 12 HOURS AFTER ADMISSION



Series 1 – less than normal

Series 2- normal

Series 3- more than normal

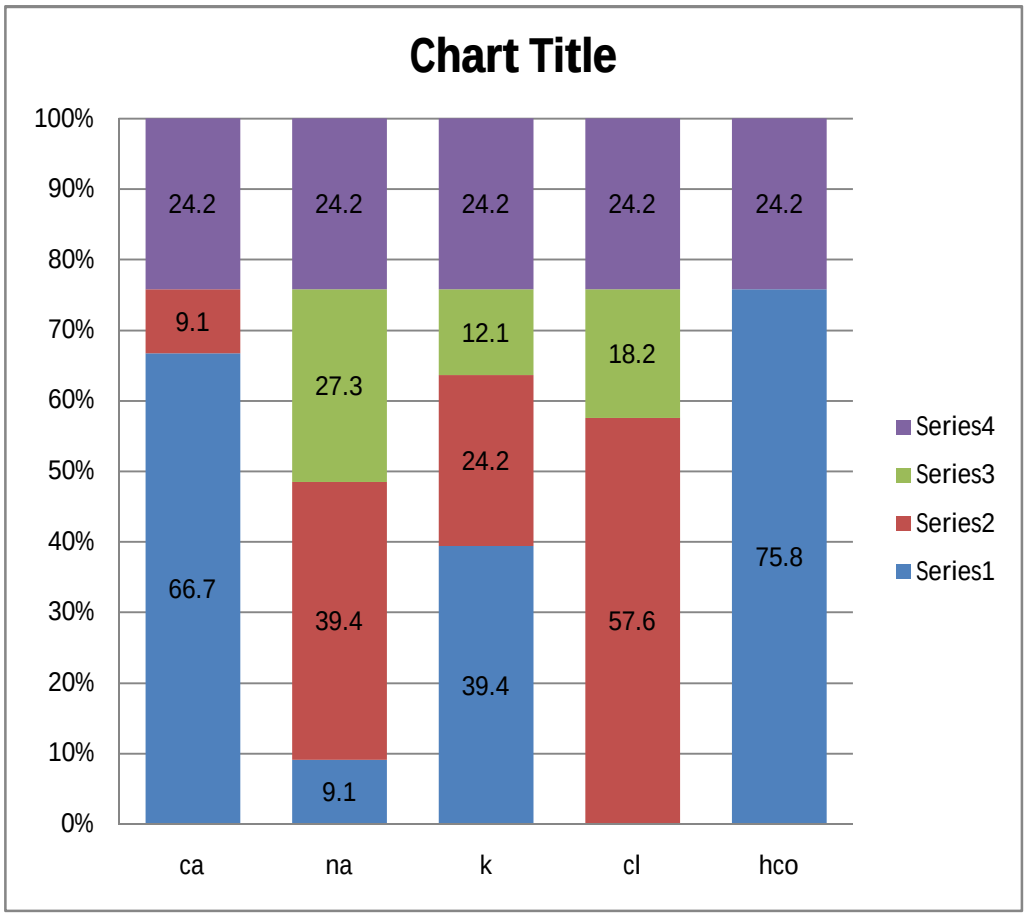
Series 4-not taken due to corrected the acidosis

In this study 12 hours after the admission patients were having

1) Calcium - 78.8% had hypocalcimia, 15.2% has normal value, 3% hypercalcimia and 3% not taken due to acidosis correction

2) Sodium- 18.2% had hyponatremia,42.4% were in normal range ,36.4% had hypernatremia and 3% not taken due to acidosis correction or death
3) Potassium-48.4% had hypokalemia, 30.3% had normal range , 18.2% were in hyperkalemia, and 3% were not taken
4) Chloride- 72.7% had normal range , 24.2% had hyperchlorimia and 3% were not taken
5) Bicarbonate- 93.9% were in acidotic range, 3% were normal and 3% were not taken

ELECTROLYTE IMBALANCES AT 24 HOURS AFTER ADMISSION



Series 1 – less than normal

Series 2- normal

Series 3- more than normal

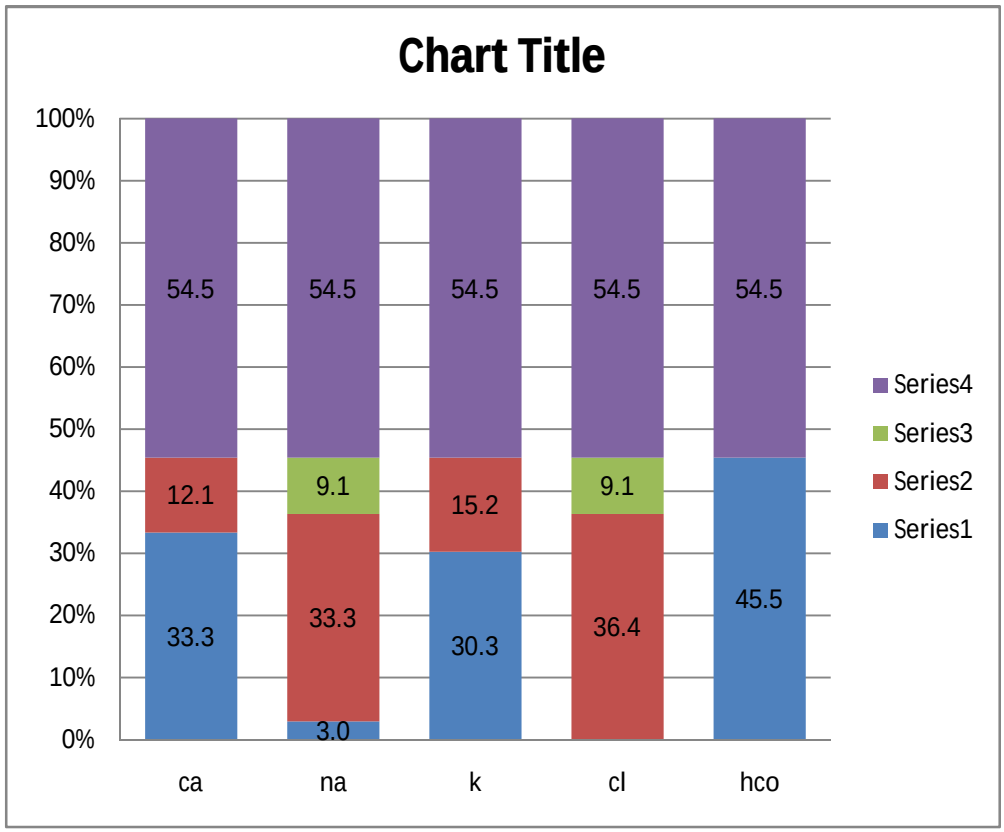
Series 4-not taken due to corrected the acidosis

In this study after 24 hours of admission patients were having

1) Calcium-66.7% had hypocalcimia ,9.1% has normal value and 24.2% not taken due to acidosis correction

2) Sodium- 9.1% had hyponatremia,39.4% were in normal range ,27.3% had hypernatremia and 24.2% not taken due to acidosis
3) Potassium-39.4% had hypokalemia, 24.2% had normal range , 12.1% were in hyperkalemia, and 24.2% were not taken
4) Chloride- 57.6% had normal range, 18.2% had hyperchlorimia and 24.2% were not taken
5) Bicarbonate t- 75.8% were in acidotic range and 24.2% were not taken

ELECTROLYTE IMBALANCES AT 36 HOURS AFTER ADMISSION



Series 1 – less than normal

Series 2- normal

Series 3- more than normal

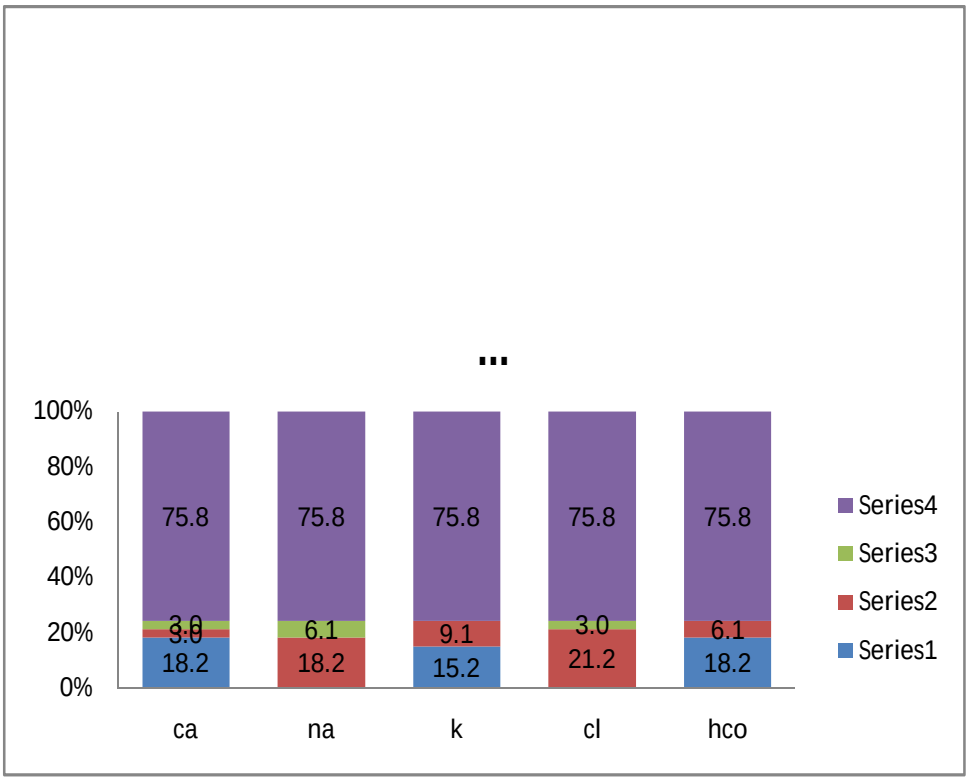
Series 4-not taken due to corrected the acidosis

In this study 36 hours after the admission patients were having

1) Calcium-33.3% had hypocalcemia, 12.1% has normal value, and 54.5% not taken due to acidosis correction

2) Sodium- 3% had hyponatremia,33,3% were in normal range ,9.1% had hypernatremia and 54.5% not taken due to acidosis
3) Potassium-30.3% had hypokalemia, 15.2% had normal range , and 54.5% were not taken
4) Chloride- 36.4% had normal range , 9.1% had hyperchlorimia and54.5% were not taken
5) Bicarbonate- 45.5% were in acidotic range, and 54.5% were not taken

ELECTROLYTE IMBALANCES AT 48 HOURS AFTER ADMISSION



Series 1 – less than normal

Series 2- normal

Series 3- more than normal

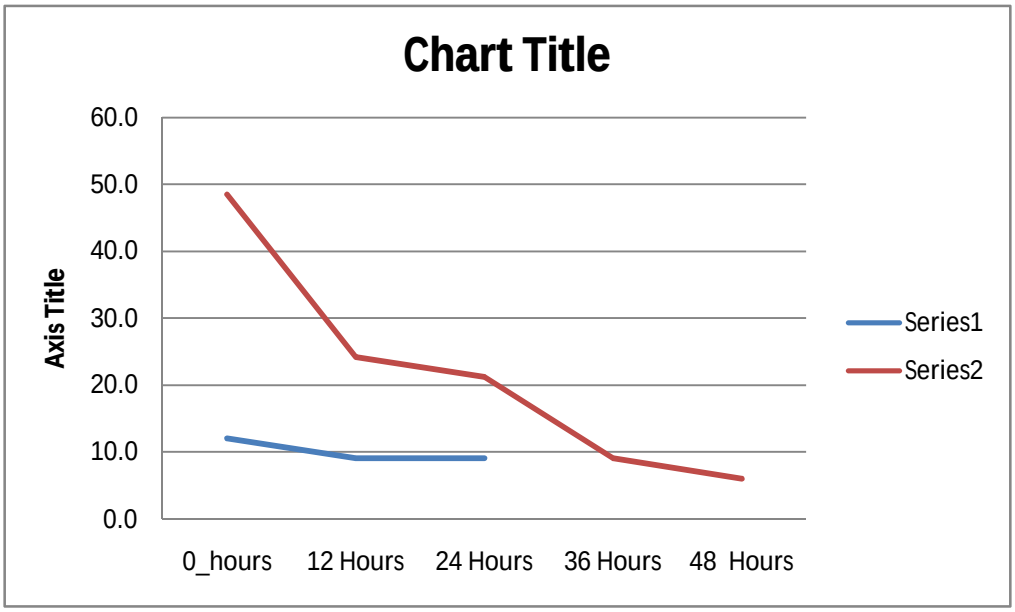
Series 4-not taken due to corrected the acidosis

In this study 48 hours after the admission patients were having

1) Calcium-18.2% had hypocalcemia, 3% has normal value and 3% were hypercalcimic and75.8% not taken due to acidosis correction or death

2) Sodium- 18.2% were in normal range, 6.1% had hypernatremia and 75.8% not taken due to acidosis correction or death
3) Potassium-15.2% had hypokalemia, 9.1% had normal range , and 75.8% were not taken due to acidosis correction or death
4) Chloride- 21.2% had normal range, 3% had hyperchlorimia and 75.8% were not taken
5) Bicarbonate- 18.2% were in acidotic range, 6.1% were in normal range and 75.8% were not taken

ABNORMAL RENAL FUNCTION AND DKA STATUS



Series 1- pre renal failure

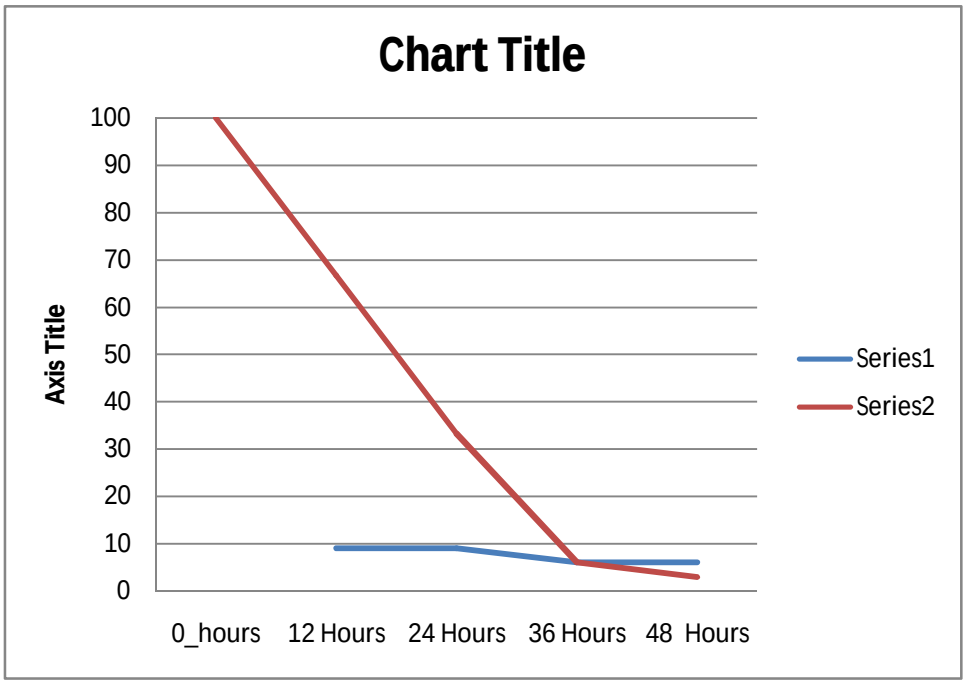
Series 2-renal failure

In this study

Pre renal failure seen in children at admission 12.1 %, at 12 hours-9.1%, at 24 hours -9.1 %, at 36 and 48 hours no pre renal failure were reported.

Renal failure seen in children at admission 48.5 %,at 12 hours-24.2%, at 24 hours – 21.2 %, at 36 hours-9.1% and 48 hours- 6.1%.

METABOLIC ACIDOSIS



Series 1- normal anion gap metabolic acidosis

Series 2-high anion gap metabolic acidosis

In this study

Normal anion gap metabolic acidosis seen in children at admission is absent, at 12 hours-9.1% ,at 24 hours -9.1 %, at 36 hours-6.1% and at 48 hours-6.1% no pre renal failure were reported.

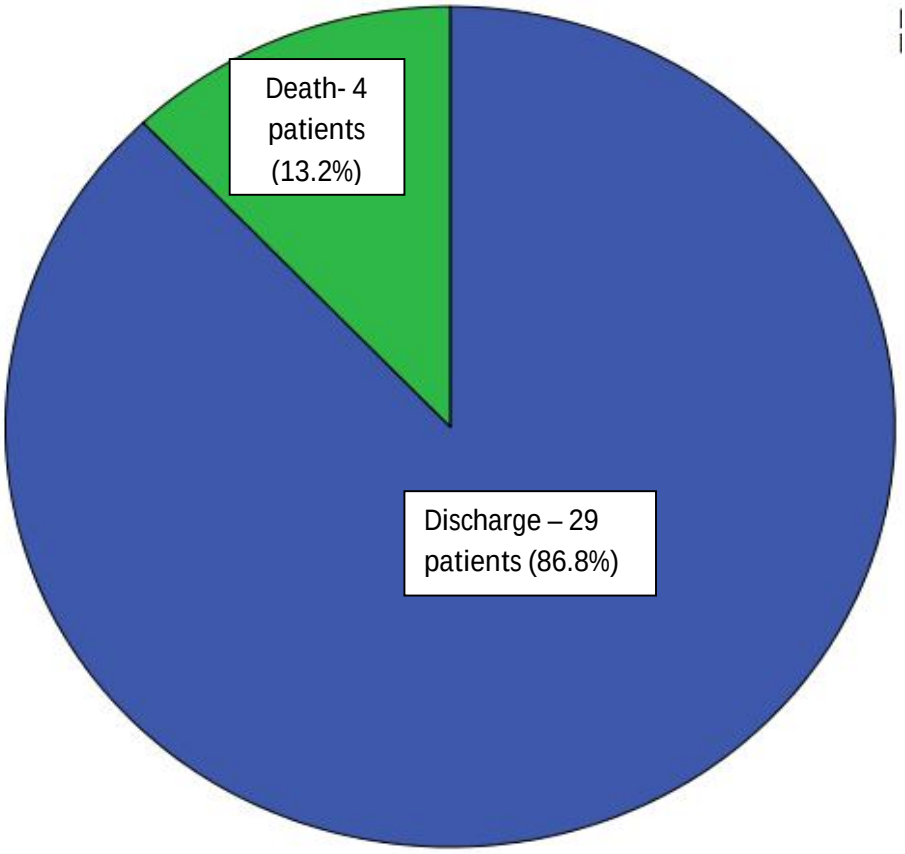
High anion gap metabolic acidosis seen in children at admission 100 %,at 12 hours-66.7% ,at 24 hours – 33.3 %, at 36 hours-6.1% and 48 hours- 3%.

INSULIN INFUSION DURATION OF DKA PATIENTS

Hours	Frequency	Percent	Cumulative Percent
<12	9	27.3	27.3
12-24	11	33.3	60.6
24-48	10	30.3	90.9
>48	3	9.1	100.0
Total	33	100.0	

In this study, 27% children recovered with insulin infusion less than 12 hours, 61% within 24 hours and 91% within 48 hours. Only 9% of children required insulin infusion beyond 48 hours.

OUTCOME IN DKA PATIENTS



1) Discharge
2) Death

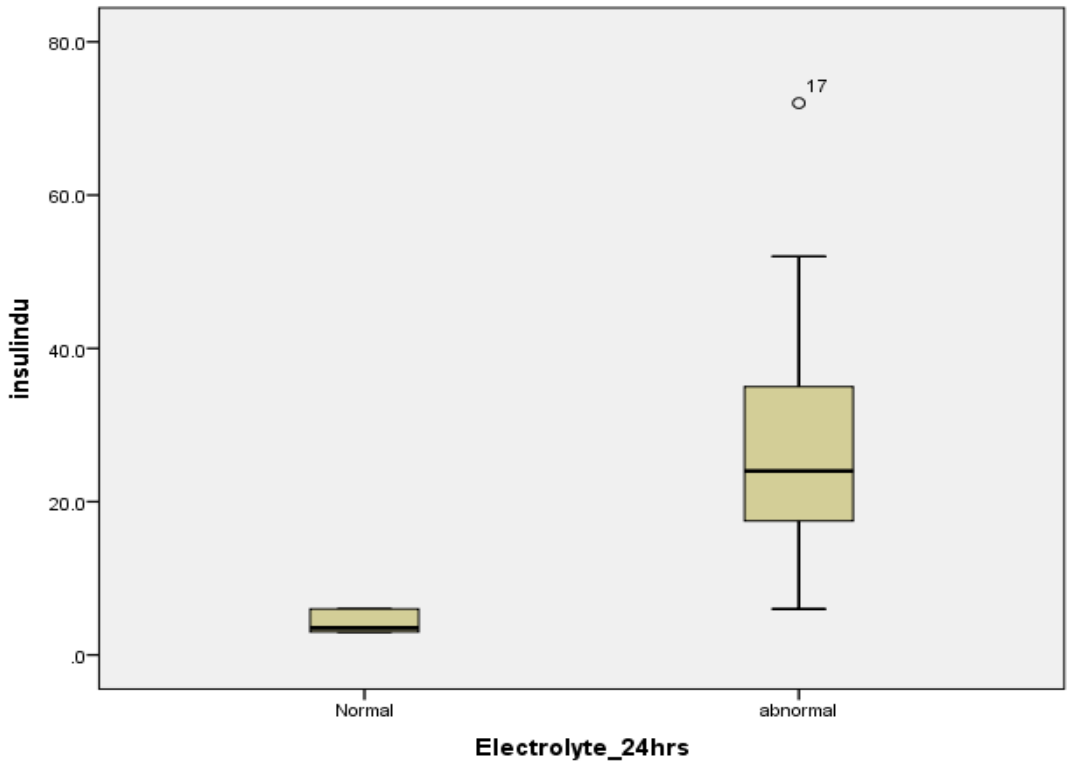
Outcome of this study mentioned as discharge which accounts 29(86.8%) and death accounts 4 (13.2%)

LENGTH OF HOSPITAL STAY OF DKA PATIENTS

Days		Frequency	Percent	Cumulative Percent
Valid	<3	0	0	0
	3-7	2	7	7
	7-14	16	55	62
	>14	11	38	100.0
	Total	29	100.0	

In this study DKA patient stayed in this hospital were <3 days- 0%,4-7 were – 2 patients(7%) , 7-14 were – 62%) and remaining takes > 14 days patients(38%)

RELATION BETWEEN METABOLIC DERRANGEMENTS AND INSULIN INFUSION DURATION IN DKA AT 24 HOURS



When the duration of insulin infusion was compared between the patients who had normal and abnormal electrolytes at 24 hours of admission the median (IQR) of former group was 3.5 (3.0) hours. While that of later group was 24 (18) hours

RELATION BETWEEN METABOLIC DERRANGEMENTS AND INSULIN INFUSION DURATION IN DKA AT 24 HOURS

Duration of insulin infusion	Electrolyte at 24hrs		Total
	Normal	abnormal	
<12	6	1	7
12.-24	0	11	11
24-48	0	9	9
>48	0	2	2
Total	6	23	29

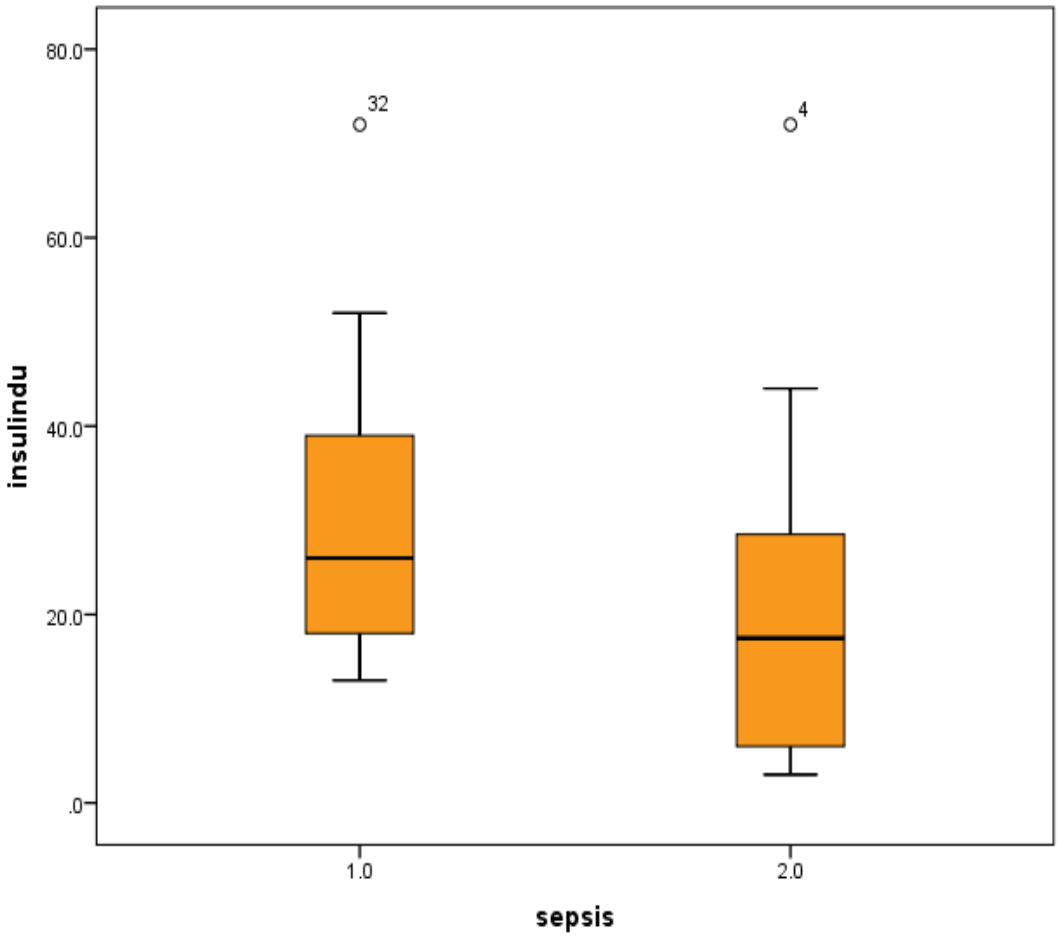
X^2 =23.776

p =< 0.001

On applying chi square test a significant reduction in duration of insulin infusion was demonstrated in children whose electrolyte levels normalised at 24 hours

When the duration of insulin infusion in patients who had normal and abnormal electrolyte at 24 hours was compared , it was found that all patients who had normal electrolyte at 24 hours required insulin infusion less than 12 hours

RELATION BETWEEN CULTURE POSITIVE SEPSIS AND INSULIN DURATION



1) Culture positive sepsis
2) Culture negative

From the above graph it is apparent that sepsis positive patients required more duration of insulin infusion compared to those without sepsis. The median (interquartile)ofinsulin infusion required for the culture positive groupis 23 (24)hours and culture negative group is 14 (25) hours.

RELATION BETWEEN CULTURE POSITIVE SEPSIS AND INSULIN DURATION

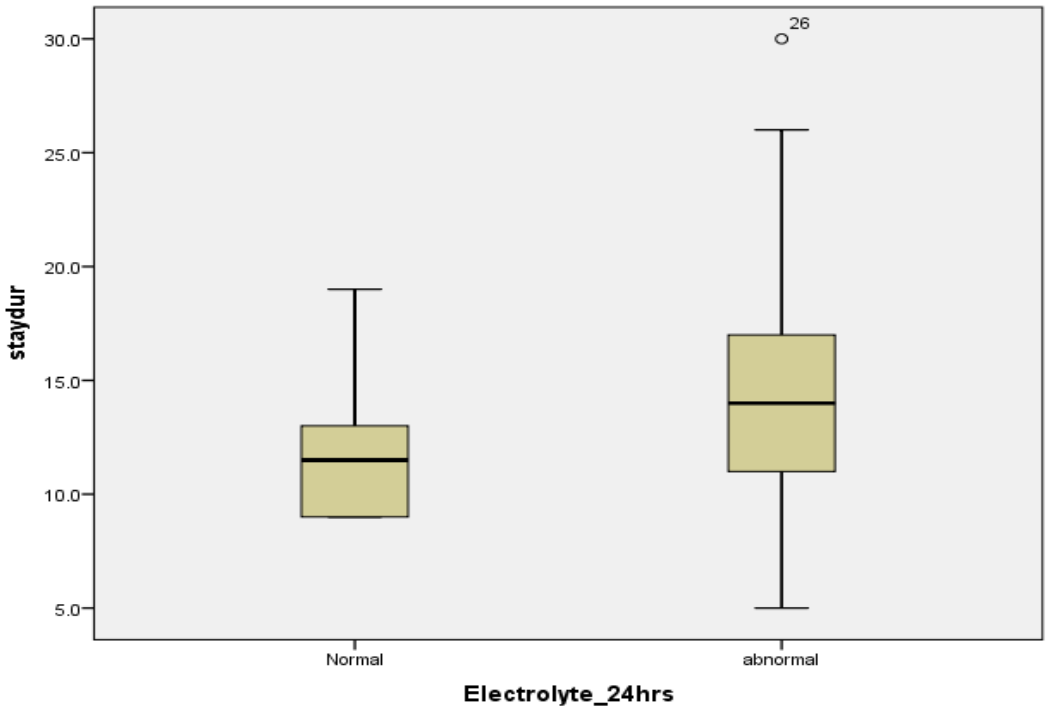
	Number	Mean	Standard Deviation
Sepsis positive	9	31.775	19.45
No sepsis	24	19.667	16.60

$p = 0.084$

By applying independent test with equal variances assumed, p value was not significant.

That is, though apparently patients with culture positive required insulin infusion for long duration, this is not statistically significant.

RELATION BETWEEN METABOLIC DERRANGEMENTS AND HOSPITAL STAY DURATION AT 24 HOURS



Median duration of stay in children who had normal electrolytes level at 24 hours was 11.5 days inter quartile range was 5.5 days and the mean was 12.1 days.

In contrast, for children who had abnormal electrolyte levels at 24 hours median duration of stay was 14 days and IQR was 8 and mean was 17.5 days.

RELATION BETWEEN METABOLIC DERRANGEMENTS AND HOSPITAL STAY DURATION AT 24 HOURS

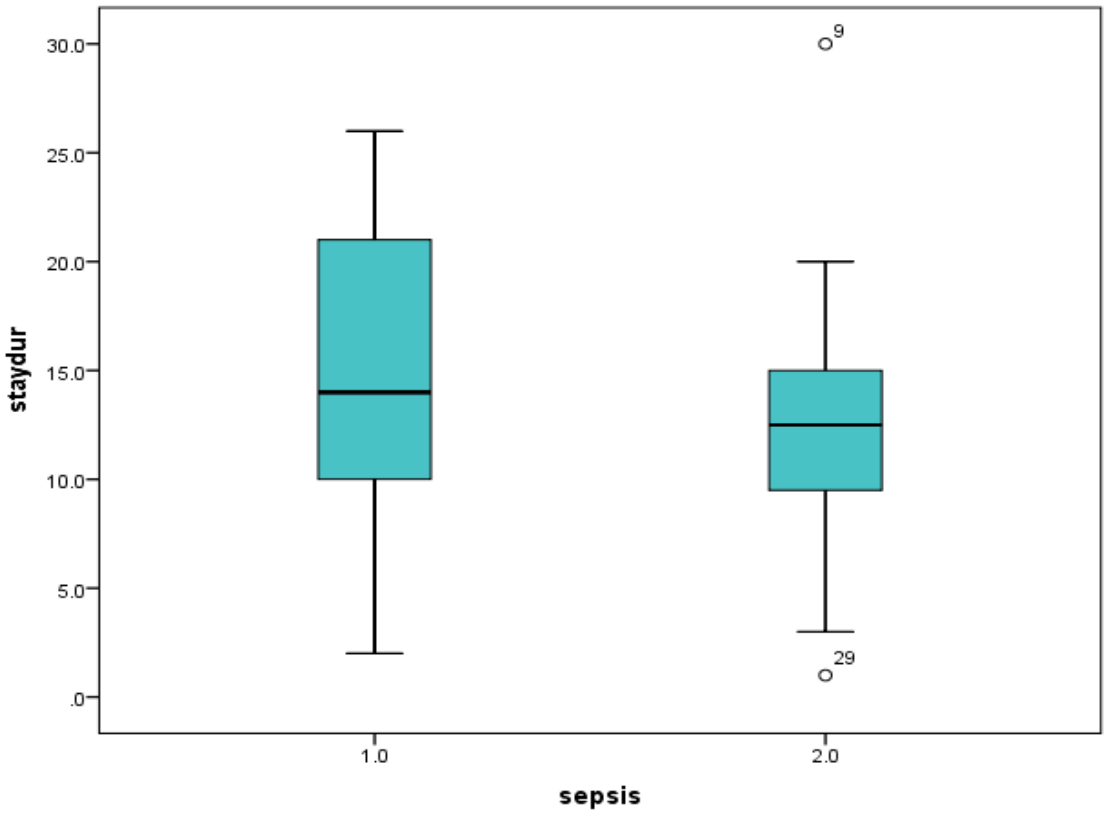
Duration	Normal		Abnormal		Total
	No	%	No	%	
<3	0	0	0	0	0
4-7	2	33	1	4	3
7-14	3	50	11	48	14
>14	1	17	11	48	13
Total	6	100	23	100	29

$X^2 = 2.51$

P= 0.28

The duration of stay is more in patients who had abnormal electrolyte level at 24 hours – Only 17 % of patients with normal electrolyte level at 24 hours stayed beyond 14 days, while 48% of patients with electrolyte disturbances persisting at 24 hours stayed beyond 14 days. But this difference was not statistically significant.

RELATION BETWEEN CULTURE POSITIVE SEPSIS AND HOSPITAL STAY DURATION



1) Culture positive sepsis
2) Culture negative

Median duration of stay in children who had culture positive sepsis was 14 days and inter quartile range was 14 days.

In contrast, for children who were culture negative median duration of stay was 13 days and IQR was 5.3 days.

RELATION BETWEEN CULTURE POSITIVE SEPSIS AND HOSPITAL STAY DURATION

	Number	Mean	Standard deviation
Culture positive	9	14.22	8.19
Culture negative	24	12.7	5.82

P= 0.557

Though the duration of stay is more in patients who had culture positive sepsis, this was not statistically not significant.

DISSCUSION

This study has brought out various electrolyte abnormalities at presentation and at various time intervals in children hospitalised for DKA.

SODIUM

In this study, at the time of admission 27.3% population were hyponatremic, 57.6% were in normal range and 15.2% had hypernatremia. The study done by Kenwal sk et al[17] observed that on the time of admission only 20% were hypernatremic. Another study done by Andrew E Edo[24] showed that about 36.9% had hyponatremia and 1.2% had hypernatremia at admission.

Serial monitoring of sodium in this study showed that with treatment hyponatremia decreased and hypernatremia increased up to 24 hours after which sodium levels gradually stabilised to normal level.

At the end of 48 hours of admission only 6.1 % patient has sodium disturbances in the form of hypernatremia. All others had normal sodium level or had their acidosis corrected / expired

POTTASSIUM

In this study at the time of admission 24.2% had hypokalemia, 45.5% had normal potassium levels and 30.3% had hyperkalemia. In a study conducted by Andrew E Edo [24] he observed that 21% had hyperkalemia at admission and only 3% had hypokalemia . Similarly study conducted by kanwal sk et al [3] showed only 14.5% had hypokalemia. Moulik et al[1] observed in their study that 59.6% were hypokalemic.

Study by moulik et al showed that there was significant fall in potassium level 6 hours after therapy with 100 % of mal nourished children and 72.7% of children with normal nutrition developing hypokalemia during therapy. This is similar to findings of our study which showed that prevelance of hypokalemia increases from 24% at admission to maximum of 48% at 12 hours. Following this potassium levels tends to normalize so that at 48 hours only 15% hypokalemia.

CHLORIDE

In this study estimation of chloride level showed that 15.2% had hyperchloremia on admission which increases to maximum of 24% at 24 hours. There after chloride level tend to normallise with only 3% had hyperchlremia at 48 hours.

CALCIUM

Hypocalcemia is common in children DKA due to volume depletion , sepsis, rhabdomylosis and hypomagnecimia.

In our study as much as 82% of patients had hypocalcemia on admission. Which decreased gradually with therapy. At the end of 48hours only 18% had hypocalcemia.

BICARBONATE

Bicarbonate levels which is the hallmark of metabolic acidosis was observed in all patients on admission. The percentage of children with low bicarbonate level gradually with treatment but 18% had low bicarbonate levels even at 48 hours after therapy.

All patient had high anion gap metabolic acidosis at presentation with treatment the number of patients with high anion gap metabolic acidosis decreased gradually with only patient to have high anion gap metabolic acidosisat the end of 48 hours . Normal anion gap metabolic acidosis was seen in 12hours and 24 hours, 6% in 36hours and 48 hours .hyperchloremia could be contributed to normal anion gap metabolic acidosis observed in this study.

RENAL FAILURE IN DKA

In this study during the time of admission 48.5% had renal failure and 9.1% had pre renal failure. A study conducted by C.F .Otieno et al[27] on adults observed that 71.5% had abnormal renal parameters . Against this Moulik et al [25] observed that only 9% had renal failure at admission.

This deranged renal function was transient as evidenced by gradual decrease in proportion of children with renal failure with treatment. At 48hours after treatment only 6% had renal failure.

It was observed in our study that most of the electrolyte disturbances were maximum at 12 hours after which they started to decline gradually.

The duration of insulin infusion and hospital stay were compared for children with normal and abnormal electrolyte at 24 hours. Children with electrolyte disturbances at 24 hours had a statistically significant longer duration of insulin infusion requirement. However this did not result in a significant prolongation of hospital stay

It was observed that out of 33 patients 9 (27%) had a culture positive sepsis. When the duration of insulin infusion and hospital stay was compared between culture positive and negative groups, though there was a slight prolongation of both in sepsis group , this was not statistically significant . there are no study with similar data available for comparison.

HIGHLIGTS

1) First of its kind to describe the electrolyte abnormality over a period of time at periodic intervals in children with DKA
2) All electrolyte measurements were done as per recommended procedures .
3) There was no missing data. All parameters were taken at appropriate time .
4) Renal parameters which have significant influence on electrolyte level were also monitored
5) Patients were followed up till discharge or death, and data on duration of insulin infusion and hospital stay were also captured .

LIMITATIONS

1) Small sample size.
2) Phosphate level not done.
3) Corrected sodium not calculated and analyse, this was to bring out the actual abnormality in patients.
4) Magnesium not done.

SUMMARY

- On admission low bicarbonate level and high anio gap metabolic acidosis was observed in all patients.
- Hypocalcemia was the commonest (82%) and hyperchloremia the rarest (15%) electrolyte disturbance observed on admission
- The proportion of patients with most electrolyte disturbances peaked at 12 hours, after which they started decline.
- More than half of the patients (60%) required insulin infusion less than 24 hours and 90% for less than 48 hours. Only 10% required insulin infusion more than 48 hours .
- As many as 2/3rd of paitents were discharged prior to 2 weeks and only 1/3rd stayed beyond 2 weeks.
- Patients with electrolyte disturbances persisting at 24 hours required insulin infusion to a significantly longer duration.

CONCLUSION

- The relative proportions of various metabolic derangements in children with DKA are described.
- Patients with electrolyte disturbances persisting at 24 hours required insulin infusion to a significantly longer duration

RECOMMENDATIONS

For practice

- Several monitoring of electrolytes on admission and at regular intervals are mandatory for any patients with DKA.
- Sepsis screening has to be done in all patients with DKA as sepsis as implication on duration therapy.

For research

- Further study with larger sample size including magnesium and phosphate level can through more light on complex electrolyte abnormalities encountered in DKA.

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ABBREVIATIONS

DM	-	Diabetes mellitus
DKA	-	Diabetic ketoacidosis
ISPAD	-	International Society for paediatric and adolescent diabetes
GH	-	Growth hormone
ALOC	-	Altered level of consciousness
HbA1C	-	Glycosylated haemoglobin
ICH & HC	-	Institute of child health
SPSS	-	Statistical package for social sciences
HCO3	-	Bicarbonate
PO2	-	Partial pressure of oxygen
HHS	-	Hyperosmolar Hyperglycaemic state

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. Hamza M
Postgraduate M.D.(Paediatrics)
Madras Medical College
Chennai 600 003

Dear Dr.Hamza M,

The Institutional Ethics Committee has considered your request and approved your study titled **"Metabolic Derangements in Paediatric Diabetic Ketoacidosis (DKA) in a tertiary care hospital" No.56012015.**

The following members of Ethics Committee were present in the meeting held on 20.01.2015 conducted at Madras Medical College, Chennai-3.

1. Dr.C.Rajendran, M.D.,	: Chairperson
2. Dr.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.R.Nandini, M.D., Inst.of Pharmacology, MMC	: Member
5. Prof.P.Ragumani, M.S., Professor, Inst.of Surgery, MMC	: Member
6. Prof.Md.Ali, M.D., D.M., Prof. & HOD of Medl.G.E., MMC	: Member
7. Prof.K.Ramadevi, Director, Inst.of Biochemistry, MMC	: Member
8. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
9. Thiru S.Rameshkumar	: Lay Person
10. Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
11. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

30/1/15

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMIT
MADRAS MEDICAL COLLEGE

DATA COLLECTION FORM

1. Study ID:

2. Name: 3. Age: 4. Sex:

5. IP no: 6. OP no:

7. Diabetic clinic number:

8. Date of admission:

9. Address & phone number:

10. Pre existing diabetes: a) Yes b) No

10.1. If yes, duration of diabetes:--------

a)<2yrs b)2-5yrs c)>5yrs

10.2. If so insulin dose (u/kg/day):--------

a)<0.5 u b)0.5-1u c)1-1.5u d)>1.5 u

10.3. Preceding HbA1C (with date):------/dt---------/ gap---------

a)<4 months b)<1yr c) long back

11. Family history of type I diabetes: a)yes b)no

12. Precipitating cause of DKA:a) infection b)insufficient insulin intake

c)stress d)none of the above

13. Anthropometry:

	Value	Category
Height		
Weight		
BMI		

14. Table:

	0		**12hr**		**24 hr**		**36 hr**		**48hr**	
	value	**interpretation**	**value**	**interpretation**	**value**	**interpretation**	**value**	**interpretation**	**value**	**interpretation**
Ca										
Na										
K										
Cl-										
HCO3-										
Urea										
Creatinin										
ABG interpretation										

14. Insulin infusion stopped _____hrs:a)<12 hrs b)12-24hrs c)24-48hrs

d)>48 hrs

15. Outcome: a) discharge b) death

16. Date of discharge:

17. Length of hospital stay:----days a)<3days b)4-7days c)1-2 wks d)>2wks

INFORMATION SHEET

Place of study: PAEDIATRIC INTENSIVE CARE UNIT, INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN, EGMORE,CHENNAI-8.

Name of Investigator :**Dr.HAMZA.M**

Name of Participant Age: Sex:

Hospital No:

Study title :METABOLIC DERANGMENTS IN PAEDIATRIC DKA IN A TERTIARY CARE HOSPITAL"

• We request your child to participate in the study

1)We carefully take history and assess the clinical parameters of your child and draw blood for sodium, potassium, chloride, bicarbonate urea ,creatinine and ABG tests in our pediatric intensive care ward. These tests require 2 ml of blood. These tests will be repeated after 12, 24,36and 48 hrs. These tests are done routinely as a part of management of DKA.

2)Your child will be treated as per unit protocol, total insulin infusion time will be noted for this study.

3)Your child will be followed up till the discharge, total days of admission will be noted for study.

4)The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

5)Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

6)The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator . Signature of parent/guardian.

Date:

INFORMED CONSENT FORM

Study place: DEPARTMENT OF DIABETOLOGY, INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN, EGMORE,CHENNAI-8.

Title of the study :"METABOLIC DERANGEMENT IN PAEDIATRIC DKA IN A TERTIARY CARE HOSPITAL."

Name of the investigator:**Dr.HAMZA.M.**

Name of the Participant: Age: Sex:

Hospital number:

1. I have read and understood this consent form and the information provided to me regarding the participation of my child in the study.

2. I have had the consent document explained to me.

3. I have been explained about the nature of the study.

4. I have been explained about my rights and responsibilities by the investigator.

5.I will allow my child to undergo clinical tests subjected during the study whole heartedly.

6. I will allow my child to cooperate with the investigator through out the study.

7. I have been advised about the risks associated with my child's participation in this study.*

8. I agree that my child will cooperate with the investigator and I will inform him/her immediately if my child suffer from some problem during the study. *

9. My child have not participated in any research study in the past.

10. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my child's future treatment in this hospital. *

11. I am also aware that the investigator may terminate my child's participation in the study at any time, for any reason, without my consent. *

12. I hereby give permission to the investigators to release the information obtained from my child as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.

13. I have understand that my child's identity will be kept confidential if my child's data are publicly presented

14. I have had my questions answered to my satisfaction.

15. I have decided my child can be participated in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

Name and signature / thumb impression of the parents/guardian

Name _____ Signature_____ Date_____ S

Name and Signature of impartial witness:

Name _____ Signature_____ Date_____

Name and Signature of the investigator or his representative obtaining consent:

Name _____ Signature_____ Date_____

தகவல் படிவம்

ஆய்விடம் : குழந்தைகள் தீவிர சிகிச்சை பிரிவு, அரசினர் குழந்தைகள் நல மருத்துவமனை, எழும்பூர், சென்னை.

ஆய்வாளர் : மருத்துவர் ஹம்சா.மா

பங்கு பெறுபவரின் பெயர் : வயது : பாலினம் :

மருத்துவமனை எண் :

ஆய்வு தலைப்பு : குழந்தை பருவ சர்க்கரை நோயில் ஏற்படும் வளர்சிதை மாற்றங்கள். உயர் சிகிச்சை மையத்தில் குழந்தை பருவ சர்க்கரை நோயில் ஏற்படும் வளர்சிதை மாற்றங்கள்.

1. உங்கள் குழந்தையிடம் நோயின் தன்மையை கேட்டறிந்து மருத்துவ அளவுரு செய்து இரத்த பரிசோதனை எடுத்து சோடியம், பொட்டாசியம், குளோரைடு, பைகார்பளேட், யூரியா கிரியாடினின் மற்றும் ஏபிஜி ஆகியவற்றை குழந்தைகளுக்கான தீவிர சிகிச்சை பிரிவில் பெறுவோம். இந்த பரிசோதனையில் 2மிலி ரத்தம் தேவை. 12,24,36,48 மணி நேரத்தில் திரும்பவும் செய்யப்படும். அனைத்து சிகிச்சை இப்பரிசோதனை தேவைப்படும்.

2. உங்கள் குழந்தைக்கு எங்கள் நெறிமுறைப்படி சிகிச்சை அளிக்கப்படும். இன்சுலின் செலுத்தும் நேரம் கண்காணிக்கப்படும்.

3. உங்கள் குழந்தை வீட்டிற்கு அனுப்பப்படும் வரை பின்பற்றப்படுவாள். எவ்வளவு நாள் மருத்துவமனையில் தங்குவாள் என்பது குறிக்கப்படும்.

4. இந்த பரிசோதனை முழுவதும் தங்களது ரகசியம் காக்கப்படும். அப்படி ஏதேனும் பிரசுரமாகவோ அல்லது தெரிவிக்கவோ செய்தால் தங்களது அடையாளங்கள் வெளிப்படுத்தப்படமாட்டாது.

5. இந்த சோதனையில் கலந்து கொள்வது தங்களது சொந்த விருப்பம். இதில் கருந்து கொள்வதா வேண்டாமா என்பதை நீங்களே முடிவு செய்யலாம். தங்கள் முடிவால் நீங்கள் பெறவேண்டிய எதுவும் தடைபடாது.

6. இந்த சிறப்பு பரிசோதனையின் முடிவில் பரிசோதனையின்போதோ பரிசோதனை முடிவு உங்களுக்கு தேவையான ஒன்றாக இருந்தால் உடனடியாக வழங்கப்படும்.

பரிசோதனையாளர்
கையொப்பம்

பெற்றோர்/காப்பாளர்
கையொப்பம்

ஆராய்ச்சி ஒப்புதல் படிவம்

பெயர் : தேதி :

வயது : மருத்துவமனை எண் :

பாலினம் :

ஆய்விடம் : குழந்தைகள் தீவிர சிகிச்சை பிரிவி அரசினர் குழந்தைகள் நல மருத்துவமனை, எழும்பூர், சென்னை மருத்துவ கல்லூரி

ஆய்வாளர் : மரு.ச. ஹம்சா.மா.

1. இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் எனக்கு முழுமையாகவும், தெளிவாகவும் விளக்கப்பட்டது.
2. எனக்கு விளக்கப்பட்ட விவரங்களை நான் புரிந்து கொண்டு, எனது குழந்தையை இந்த ஆராய்ச்சிக்கு உட்படுத்த சம்மதிக்கிறேன்.
3. இந்த ஆராய்ச்சியின் தன்மைகளும், எனது உரிமைகளும் எடுத்துரைக்கப்பட்டது.
4. நீரிழிவு அமில தேக்கம் உள்ள குழந்தைகளில் வளர்சிதை மாற்ற அமில தேக்கம் கண்டறியும், இந்த ஆய்வில் குழந்தையை பங்கு பெற சம்மதம் தெரிவிக்கிறேன்.
5. நான் எனது குழந்தையின் முந்தைய மற்றும் தற்போதைய மருத்துவ விவரங்களை ஆய்வாளரிடம் தெரிவித்து விட்டேன்.
6. இந்த ஆய்வினால் எற்படும் ஆபாயங்களைப் பற்றி எனக்குத் தெரிவிக்கப்பட்டது.
7. எனக்கு குழந்தையின் உடல்நலம் பாதிக்கப்பட்டாலோ (அ) வழக்கத்திற்கு மாறாக நோய்குறி தென்பட்டாலோ உடனே அதை ஆய்வாளரிடம் தெரிவிப்பேன் என உறுதியளிக்கிறேன்.
8. நான் எனது குழந்தையை இந்த ஆய்வில் தன்னிச்சையாக எந்த நிர்பந்தம் இன்றியும் பங்கேற்ற அனுமதிக்கிறேன் எந்த காரணத்தினாலும், எந்த காலகட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இந்த ஆய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.
9. நான் இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும், அதை பிரசுரிக்கவும் என முழுமனதுடன் சம்மதிக்கிறேன்.

பெற்றோர் / பாதுகாவலரின் பெயர் ஆய்வாளர் கையொப்பம்

மற்றும் கையொப்பம் மரு.அம்சா ம

தேதி :

இடம் :

MASTER CHART

study no	age	age cat	sex	pre exist	duration	dose cat	a1c cat	a1c gap	f/h	ppt cause	h/acat	w/a cat	bmi/ a	ca 0	ca @12	ca @ 24	ca @ 36	ca @ 48	na @ 0	na @ 12	na @24	na@ 36	na @ 48	k @ 0
1	12	4	1	2					2	1	2	2	2	1	1	1	4	4	1	1	1	4	4	1
2	12	4	1	2					1	1	2	1	2	1	1	1	4	4	2	2	3	4	4	2
3	4	2	1	2					2	4	1	1	2	2	3	1	1	4	1	2	2	1	4	2
4	10	4	2	2					1	4	2	2	2	1	1	1	1	1	3	3	3	2	2	1
5	5	2	2	2					2	4	1	1	2	2	1	1	1	4	2	1	2	2	4	2
6	11	4	2	1	2	3	2	3	1	4	2	2	2	1	1	1	2	4	2	3	2	2	4	3
7	12	4	2	1	2	2	2	2	2	1	2	1	2	1	1	1	4	4	2	2	1	4	4	1
8	11	4	2	2					1	1	2	2	2	1	1	1	1	4	3	3	2	2	4	2
9	4	2	2	2					2	1	2	1	2	2	1	2	1	1	2	3	2	2	3	1
10	12	4	1	2					2	4	1	2	2	1	1	1	4	4	2	3	3	4	4	1
11	11	4	2	2					1	1	2	1	2	1	1	1	1	1	1	1	1	2	2	2
12	12	4	2	2					2	1	1	1	2	1	2	4	4	4	2	3	4	4	4	2
13	6	3	1	2					2	1	2	2	2	1	1	1	1	4	2	2	2	2	4	2
14	9	3	2	1	3	3	2	2	2	2	1	2	2	1	1	1	4	4	1	1	2	4	4	3
15	1 1/2	2	1	1					2	4	2	1	2	1	2	4	4	4	3	3	4	4	4	3
16	10	4	1	2					1	1	2	2	2	1	2	2	4	4	2	2	3	4	4	3
17	12	4	2	1	2	4	2	3	2	2	1	2	2	1	1	4	4	4	2	3	4	4	4	2
18	10	4	1	2					1	4	2	2	2	1	1	4	4	4	1	2	4	4	4	2
19	12	4	1	2					1	4	1	2	2	2	1	1	2	1	3	3	3	3	2	1
20	5	2	2	2					2	4	2	2	2	1	1	4	4	4	2	2	4	4	4	2
21	6	3	1	2					2	4	2	2	2	1	1	4	4	4	2	1	4	4	4	1
22	9	3	1	1	1	3	3	1	1	1	2	2	2	1	1	2	2	1	2	3	3	2	2	2
23	1 1/2	2	1	2					2	1	2	2	2	2	2	1	1	3	2	3	3	2	2	3
24	55	1	1	2					2	1	2	1	2	1	1	1	1	2	2	2	2	2	2	3
25	12	4	2	1	2	3	3	1	2	2	2	2	2	1	1	1	4	4	1	2	2	4	4	2
26	10	4	1	1	1	3	3	1	2	4	1	1	2	1	1	1	1	4	1	2	2	3	4	2
27	12	4	2	1	2	3	3	1	2	4	1	2	3	1	1	1	4	4	2	2	3	4	4	1
28	6	3	2	1	2	2	3	1	2	4	2	2	2	2	1	1	4	4	2	2	2	4	4	2
29	2 1/2	2	1	2					2	4	2	2	2	1	4	4	4	4	1	4	4	4	4	3
30	12	4	2	1	1	4	3	1	2	4	2	2	2	1	1	1	1	4	2	2	2	2	4	3
31	1 1/4	2	2	1	1	2	3	1	2	1	2	2	2	1	1	1	4	4	1	1	2	4	4	2
32	1/4	1	1	1	1	2	2	1	2	1	2	1	2	1	2	1	2	1	3	3	3	3	3	3
33	6	3	1	2					2	4	1	1	2	1	1	4	4	4	2	2	4	4	4	3

MASTER CHART

k @ 12	k @24	k @ 36	k @ 48	cl- @ 0	cl- @ 12	cl- @ 24	cl- @ 36	cl- @ 48	hco3- @ 0	hco3-@12	hco3-@24	hco3-@36	hco3-@48	urea @0	urea@ 12	urea@ 24	urea@ 36	urea@ 481	creat@0	creat@12	creat@24
1	1	4	4	2	2	2	4	4	1	1	1	4	4	2	1	1	4	4	1	1	1
2	2	4	4	2	2	2	4	4	1	1	1	4	4	1	1	1	4	4	1	1	1
3	2	2	4	2	2	2	2	4	1	1	1	1	4	1	1	1	1	4	2	1	1
1	1	1	1	2	3	3	3	2	1	1	1	1	1	2	2	2	1	1	2	2	2
1	1	2	4	2	2	2	2	4	1	1	1	1	4	1	1	1	1	4	1	1	1
1	1	2	4	2	2	2	2	4	1	1	1	1	4	2	2	1	1	4	2	2	2
2	1	4	4	2	2	2	4	4	1	1	1	4	4	1	1	1	4	4	1	1	1
1	1	1	4	2	3	2	2	4	1	1	1	1	4	1	1	1	1	4	2	2	2
1	1	1	1	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1
1	2	4	4	2	2	2	4	4	1	1	1	4	4	2	2	1	4	4	2	2	2
1	2	1	1	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	2	1	1
2	4	4	4	2	3	4	4	4	1	1	4	4	4	2	1	4	4	4	2[1]	1	4
1	1	1	4	2	2	2	2	4	1	1	1	1	4	2	1	1	1	4	1	1	1
3	3	4	4	2	2	2	4	4	1	1	1	4	4	1	1	1	4	4	2	1	1
2	4	4	4	3	2	4	4	4	1	1	4	4	4	2	1	4	4	4	1	1	4
3	3	4	4	2	3	3	4	4	1	1	1	4	4	2	2	2			2	2	2
1	4	4	4	2	2	4	4	4	1	1	4	4	4	1	1	4			1	1	
2	4	4	4	2	2	4	4	4	1	1	4	4	4	1	1	4			1	1	
1	1	1	1	2	3	3	2	2	1	1	1	1	1	2	2	2	1	1	2	1	1
2	4	4	4	2	2	4	4	4	1	2	4	4	4	1	1	4			1	1	
1	4	4	4	2	2	4	4	4	1	1	4	4	4	1	1	4			1	1	
3	3	2	2	2	2	2	2	2	1	1	1	1	2	1	1	1	1	1	1	1	1
1	1	1	1	3	3	2	3	2	1	1	1	1	2	2	2	1	1	1	2	2	1
2	2	1	2	3	3	3	2	2	1	1	1	1	1	2	2	2	1	1	1	1	1
1	2	4	4	2	2	3	4	4	1	1	1	4	4	1	1	1			2	1	1
1	1	1	4	2	2	2	2	4	1	1	1	1	4	1	1	1	1		2	1	1
2	2	4	4	2	2	2	4	4	1	1	1	4	4	1	1	1			2	2	2
2	1	4	4	2	2	2	4	4	1	1	1	4	4	2	1	1			2	1	1
4	4	4	4	2	4	4	4	4	1	4	4	4	4	1	4	4			1		
3	3	2	4	3	2	2	2	4	1	1	1	1	4	2	2	2	1		2	2	2
1	1	4	4	2	2	2	4	4	1	1	1	4	4	1	1	1			1	1	1
3	2	1	2	3	3	3	3	3	1	1	1	1	1	2	2	2	2	2	1	2	2
2	4	4	4	2	2	4	4	4	1	1	4	4	4	1	1	4			1	1	

MASTER CHART

creat@36	creat@48	rftcat@0	rft cat@12	rftcat@24	rftcat@36	rftcat@48	abg @0	abg@12	abg@24	abg@36	abg@48	insulin du	insulin cat	stay dur	stay cat	outcome	sepsis
4	4	1	3	3			2	1	3			15	2	21	4	1	1
4	4	2	3	3			2	2	3			13	2	10	3	1	1
1	4	2	3	3	3		2	1	1	3		18	2	16	4	1	2
2	2	2	2	2	2	2	2	2	2	1	1	72	4	13	3	1	2
1	4	3	3	3	3		2	2	2	3		30	3	12	3	1	2
1	4	2	2	2	3		2	2	3	3		35	3	18	4	1	2
4	4	3	3	3			2	2	3			23	2	5	2	1	1
1	4	2	2	2	3		2	2	2	3		35	3	12	3	1	2
1	1	3	3	3			2	2	2	3	3	44	3	30	4	1	2
4	4	2	2	2			2	2	1			24	2	8	3	1	2
1	1	2	3	3	3	3	2	2	1	1	1	52	4	14	4	1	1
4	4	2	3				2	3				6	1	19	4	1	2
1	4	1	3	3			2	2	3	3		17	2	15	3	1	2
4	4	2	1	1			2	1	3			17	2	7	2	1	2
4	4	1	3				2	3				7	1	3	1	2	2
		2	2	2			2	2	2			26	3	2	1	2	1
		3	3				2	3				3	1	9	3	1	2
		3	3				2	3				3	1	12	3	1	2
1	1	2	1	1	3	3	2	2	2	3	3	35	3	13	3	1	2
		3	3				2	3				4	1	13	3	1	2
		3	3				2	3				6	1	9	3	1	2
1	1	3	3	3	3	3	2	2	2	3	3	28	3	14	3	1	1
1	1	2	2	3	3	3	2	2	3	3	3	19	2	20	4	1	2
1	1	1	1	1	3	3	2	2	2	2	3	39	3	24	4	1	1
		3	3	3			2	2	3			6	1	15	4	1	2
1		2	3	3	3		2	2	2	3		25	3	15	4	1	2
		3	3	3			2	2	3			14	2	10	3	1	2
		2	3	3			2	2	3			18	2	10	3	1	2
		3					2					4	1	1	1	2	2
2		2	2	2	2		2	2	2	3		27	3	14	3	1	2
		3	3	3			2	2	3			18	2	26	4	1	1
2	2	2	2	2	2	2	2	2	2	2	2	72	4	12	3	2	1
		3	3				2	3				3	1	11	3	1	2